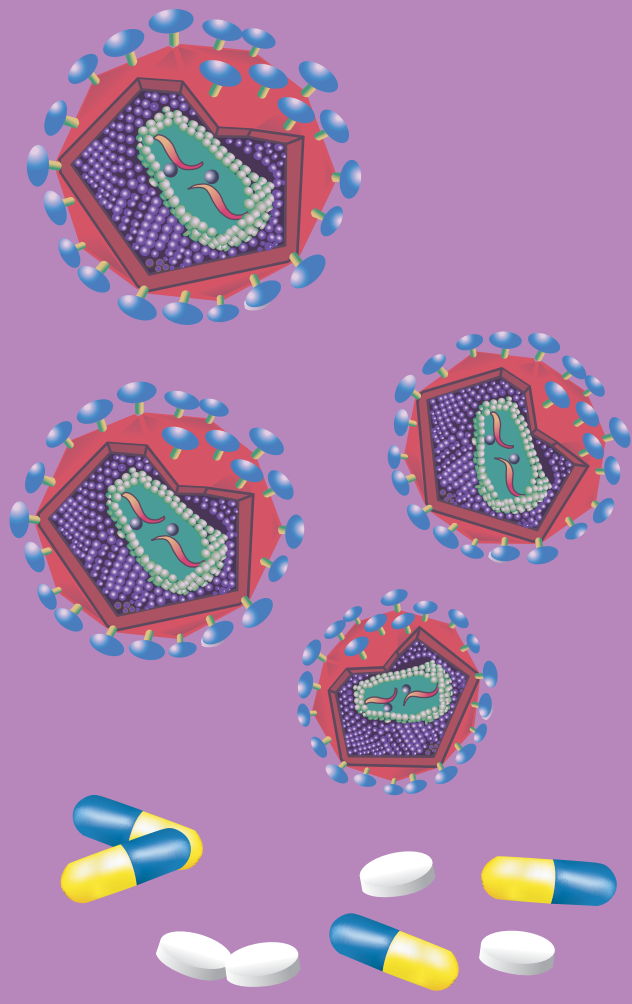
Antiretroviral Therapy Guidelines for HIV-Infected Adults and Adolescents Including Post-exposure Prophylaxis



May 2007

NACO

Ministry of Health & Family Welfare
Government of India

Assessment and Management of HIV-Infected Person

Is HIV infection confirmed?

No → Send to ICTC for confirmation of HIV status

Yes

- Perform history taking and physical examination *(see p 9)*
- Evaluate for signs and symptoms of HIV infection or OIs and WHO clinical staging *(see p 10)*
- Provide appropriate investigations/treatment of OIs *(see p 13)*
- If pregnant, refer to PPTCT
- Screen for TB
- Screen for STI

Identify need for:

- CTX prophylaxis *(see p 16)*
- ART *(see p 18)*

No → Pre ART care *(see p 15)*

Yes

- Give patient education on treatment and adherence *(see p 54)*
- Arrange psychosocial, nutrition and community support **(***see p 56***)**
- Start ART, *(see p 19)*
- Arrange follow-up + monitoring *(see p 25)*
- Assess adherence every visit
- Provide positive prevention advice and condoms
- Provide patient information sheet on the ART regimen prescribed *(see annex 7, 8)*

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with support from
CDC . Clinton Foundation . WHO

K. Sujatha Rao
Additional Secretary & Director General
National AIDS Control Organisation, Ministry of Health and Family Welfare, Government of India

FOREWORD

The HIV/AIDS epidemic is nearly 26 years old. The initial years of response to infection were focused mainly on prevention activities. As the information about the structure, molecular biology and pathogenesis of HIV has increased, the focus has shifted towards developing newer antiretroviral drugs & treatment strategies.

Though, antiretroviral therapy (ART) does not cure HIV/AIDS, but effective antiretroviral regimens inhibit the efficient replication of the HIV virus, and reduce viremia to undetectable levels. This leads to slowing of disease progression and fewer opportunistic infections and helps people lead more productive lives, with perceptibly reduced stigma and discrimination. Successes achieved by ART in terms of delaying the onset of AIDS have transformed the common perception about HIV from being a "virtual death sentence" to a "chronic manageable illness".

The free ART initiative in India was launched on 1st April, 2004. The technical guidelines were modified from "WHO guidelines for ART in resource constraints settings" during a national consultation held in January 2004. As the global experience has increased over last few years, there have been changes in timing of initiation of ART, what to use and monitoring mechanisms. Hence a need was felt to revise the 2004 guidelines. A technical committee was constituted at NACO in December, 2005 to revise these guidelines. The subgroup on ART had two consultation followed by a number of e-mail consultation with national and international experts. The final guidelines have again being modified in view of revised WHO 2006 ART guidelines.

The National AIDS Control Organisation would like to acknowledge the technical and funding support provided by the WHO Country Office (India) and CDC India in the development of these guidelines.

Our special thanks go to : Dr. S. Rajasekaran (GHTM), Dr Alaka Despande (JJ Hospital), Dr BB Rewari (NACO), Dr Ajay Wanchu (PGI Chandigarh), Dr Naweet Wig (AIIMS) and Dr Polin Chan (WHO India), who were responsible for coordinating and developing these guidelines. These guidelines have not only helped to standardise the treatment protocol for adults and adolescents, but is a culmination of landmark efforts to provide comprehensive guidance to persons working in care and treatment of people living with HIV/AIDS.

Our thanks also go to: Dr N. Kumarasamy, Dr S. Subramanian, Dr Sanjay Pujari, Dr Atul Patel, Dr R Sajith, Dr. Dilip Mathai, Dr. S. Tripathy, Dr. Emmanuel, Dr. G.D Ravindran, Dr. R.R. Gangakhedkar, Dr. Priyokumar , Dr S.K. Guha, Dr SC Sharma, Dr Shyam Sunder, Dr Dora Warren, Dr. Padmini Srikantiah, Dr Puneet Diwan, Dr Fraser Wares, Dr Sahu Suvanand, Dr K. Karthikeyan, Dr V. Purohit, Dr G. Manoharan, Dr S. Subramanian, Ms. Rohini Ramamurthy.

(K. Sujatha Rao)

9th Floor, Chandralok Building, 36 Janpath, New Delhi - 110001 Phone : 011-23325331 Fax : 011-23731746
E-mail : asdg@nacoindia.org

TABLE OF

CONTENTS

ACRONYMS AND ABBREVIATIONS

ABC	abacavir
AEB	accidental exposure to blood
AFB	acid-fast bacilli
AIDS	acquired immuno deficiency syndrome
ALT	alanine aminotransferase
ART	antiretroviral therapy
ARV	antiretroviral (drug)
AST	aspartate aminotransferase
ATV	Atazanavir
AZT	zidovudine (also known as ZDV)
bid	twice daily
CD4	T-lymphocyte CD4+
CII	Confederation of Indian Industry
CNS	central nervous system
CPK	creatinine phosphokinase
CPT	cotrimoxazole preventive therapy
CXR	chest X-ray
d4T	stavudine
ddI	didanosine
DGHS	Director General of Health Services
EFV	efavirenz
FBC	full blood count
FDC	fixed-dose combination
FTC	emtricitabine
GI	gastro intestinal
HB	haemoglobin
HBV	hepatitis B virus
HCV	hepatitis C virus
HCP	health care personnel
HIV	human immunodeficiency virus
HIVDR	HIV drug resistance
IFN	interferon
IND	indinavir
IRS	immune reconstitution syndrome
NACO	National Aids Control Organization
NFV	nelfinavir
NNRTI	non-nucleoside reverse transcriptase inhibitor
NRTI	nucleoside analogue reverse transcriptase inhibitor
NVP	nevirapine
OPIM	other potentially infectious material
PCP	*pneumocystis jiroveci (carinii)* pneumonia
PCR	polymerase chain reaction
PGL	persistent generalized lymphadenopathy
PI	protease inhibitor
PLHA	people living with hiv/aids
PMTCT	prevention of mother-to-child transmission (of HIV)
PPTCT	prevention of parent-to-child transmission (of HIV)
/r	low-dose ritonavir
RBV	ribavirin
RNA	ribonucleic acid
SACS	State Aids Control Society
SQV	saquinavir
TB	tuberculosis
TDF	tenofovir disoproxil fumarate
TLC	total lymphocyte count
WHO	World Health Organization

Chapter 1

Introduction

1.1 Since the beginning of the human immunodeficiency virus (HIV) epidemic, more than 60 million people have been infected globally and as on December 2006, nearly 39 million people were living with HIV/AIDS worldwide. During the initial years, the major focus of attention was on prevention activities, followed by "care and support" of infected individuals, particularly those suffering from opportunistic infections (OIs). Over the past decade, there has been a tremendous increase in our understanding of molecular biology and the viral structure and pathogenesis of the disease. This knowledge has led to the development of a number of new antiretroviral drugs and treatment protocols. The demonstration of efficacy of these drugs in containing viral replication has changed the world's outlook on HIV/AIDS from a "virtual death sentence" to a "chronic manageable disease". Although antiretroviral therapy (ART) does not cure HIV infection, the decrease in the viral load and the improvement in immunological status brought about by the use of these drugs have resulted in a marked decrease in the mortality and morbidity associated with the disease. Earlier, the high cost of the complicated treatment regimens and the absence of basic health infrastructure were repeatedly cited as potentially insurmountable barriers.

The "Call to Action" on HIV/AIDS at the UN General Assembly Special Session (June 2001) pushed forward a new global consensus on the need for ART. In April 1992 WHO released guidelines for the use of ART in resource-constrained settings, added 10 ARV drugs to its list of "essential medicines", and for the first time, through the WHO Prequalification Project, identified a number of generic manufacturers. In September 2003 WHO declared the lack of access to antiretroviral (ARV) treatment for HIV/AIDS a "global health emergency". An emergency plan was announced to scale up access to ARV treatment in order to cover at least three million people by the end of 2005. This joint WHO/UNAIDS announcement popularly came to be known as the "3 by 5" initiative. The WHO guidelines for "Antiretroviral Use in Resource-constrained Settings" have since been revised in December 2003 and in August 2006. A subsequent amendment on the dose of stavudine (d4T) was issued by WHO in April 2007.

Phase II of the National AIDS Control Programme of the Government of India, initiated in 1999, had a component of "care and support" for HIV-infected persons, with an emphasis on universal precautions, management and prophylaxis of OIs, and provision of post-exposure prophylaxis (PEP) to health care providers. There has been a paradigm shift in the National AIDS Control Programme of India and, along with prevention and the improvement of the health care infrastructure for the delivery of care and support, treatment is now perceived as a critical component of a comprehensive programme to combat HIV/AIDS. The Government of India launched the free ART programme on 1 April 2004, starting with eight tertiary-level government hospitals in the six high-prevalence states of Andhra Pradesh, Karnataka, Maharashtra, Tamil Nadu, Manipur and Nagaland, as well as the NCT of Delhi. In Phase I of the implementation of this programme, the subgroups of the people living with HIV/AIDS (PLHA) targeted on a priority basis were: (i) sero-positive mothers who have participated in the prevention of parent-to-child transmission (PPTCT) programme; (ii) sero-positive children below the age of 15 years; and (iii) people with AIDS who seek treatment in government hospitals. The ART centres are being scaled up in a phased manner and it is planned that free ART will be provided

to 100,000 patients by the end of 2007 and 300,000 patients by 2011 in 250 centres across the country.

The free ART programme has adopted the public health approach to administration and distribution of ART. This implies a comprehensive prevention, care and treatment programme, with a standardized, simplified combination of ART regimens, a regular secure supply of good-quality ARV drugs, and a robust monitoring and evaluation system. The public health approach for scaling up ART aims to provide care and treatment to as many people as possible, while working towards universal access to care and treatment.

The selection of first-line regimens is determined on the basis of a number of considerations, such as potency, profile of side-effects, ability to keep future treatment options open, ease of adherence, cost, risk during pregnancy and potential of the development of resistant viral strains. The current global recommendation in all circumstances is a triple drug regimen.

1.2 The **key goals** of the national ART programme include:

- To provide long-term ART to eligible patients
- To monitor and report treatment outcomes on a quarterly basis
- To attain individual drug adherence rates of 95% or more
- To increase life span so that 50% of patients on ART are alive 3 years after starting the treatment
- To ensure that 50% of patients on ART are engaged in or can return to their previous employment

1.3 **Eligibility for ART:** The national programme offers ART to the following groups of persons.

- All persons with HIV infection who are clinically eligible to receive ART
- Those who are already on ART (outside the national programme) and want to enrol with the national programme for the available ART regimens, after written informed consent

Strengthening of linkages and referrals to the prevention of parent-to-child transmission (PPTCT) programme is being carried out so that women and children living with HIV/AIDS have greater access to treatment. The national programme will also link with other programmes, such as the Revised National Tuberculosis Control Programme (RNTCP), Reproductive and Child Health (RCH) Programme and National Rural Health Mission (NRHM).

2 Chapter

Objectives of the Guidelines

These guidelines are intended to assist physicians prescribing ART, as well as the teams in the ART centres, with the practical issues regarding the treatment of HIV/AIDS. They contain recommendations to be used in the framework of the national programme as well as in dealing with special cases, in view of the role of the private sector in the provision of ART.

These guidelines were finalized in December 2003 and updated in August 2004 after national consultation with clinicians and medical practitioners from the public and private sectors, technical experts from the Director General of Health Services (DGHS), Government of India, WHO and other UN agencies, bilateral donors, Confederation of Indian Industry (CII), pharmaceutical industries, Network of Positive People and nongovernmental organizations (NGOs) involved in the care and treatment of PLHA. In December 2005, a Technical Committee on ART was constituted at NACO and seven subgroups were formed to update the guidelines on different aspects of ART. The present guidelines have been finalized after three meetings of the ART technical subgroup and online consultations with national and international experts on ART. These guidelines will continue to evolve according to the evidence and data available nationally as well as globally and will be updated regularly.

These guidelines are part of a series of NACO guidelines:

- National ART guidelines, including PEP
- National guidelines on PEP
- National guidelines for PPTCT
- National guidelines for management of OIs
- National guidelines for care and treatment of children

A

Section

MANAGEMENT *of* ANTIRETROVIRAL THERAPY *for* ADULTS *and* ADOLESCENTS

A1 Section

Diagnosis of HIV Infection in Adults and Adolescents

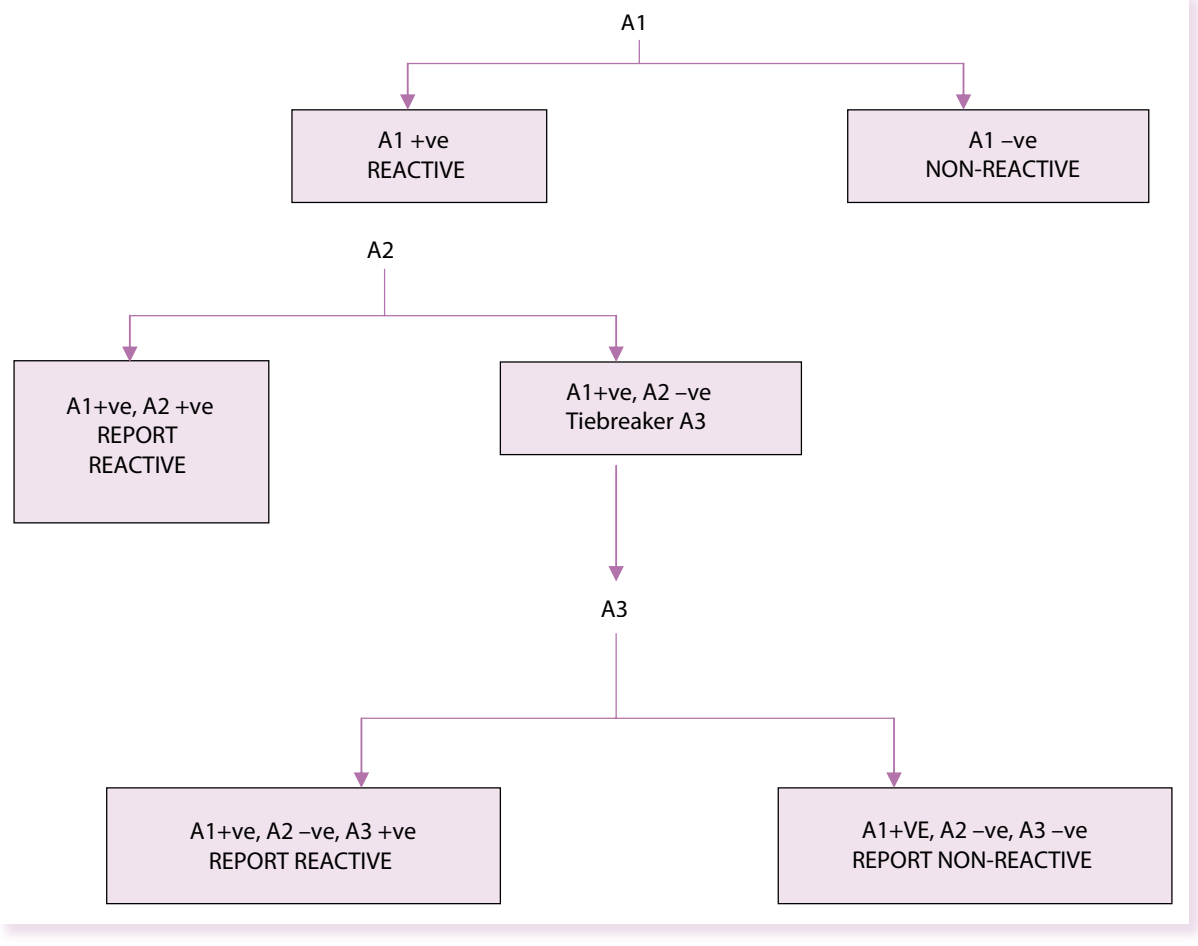
Confirmatory diagnosis of HIV infection is essential for ensuring access to care and treatment services. It is recommended that if there is any doubt regarding the diagnosis of HIV, the individual should be referred to the integrated counselling and treatment centre (ICTC) for confirmatory testing and diagnosis. An excerpt from the national strategies on HIV testing follows.

1.1 National Guidelines on Testing Adults

- For symptomatic persons: the sample should be reactive with two different kits.
- For asymptomatic persons: the sample should be reactive with three different kits
- The blood sample collected at one time is tested with the first kit. If it is reactive, it is then retested sequentially with the second and third kits.

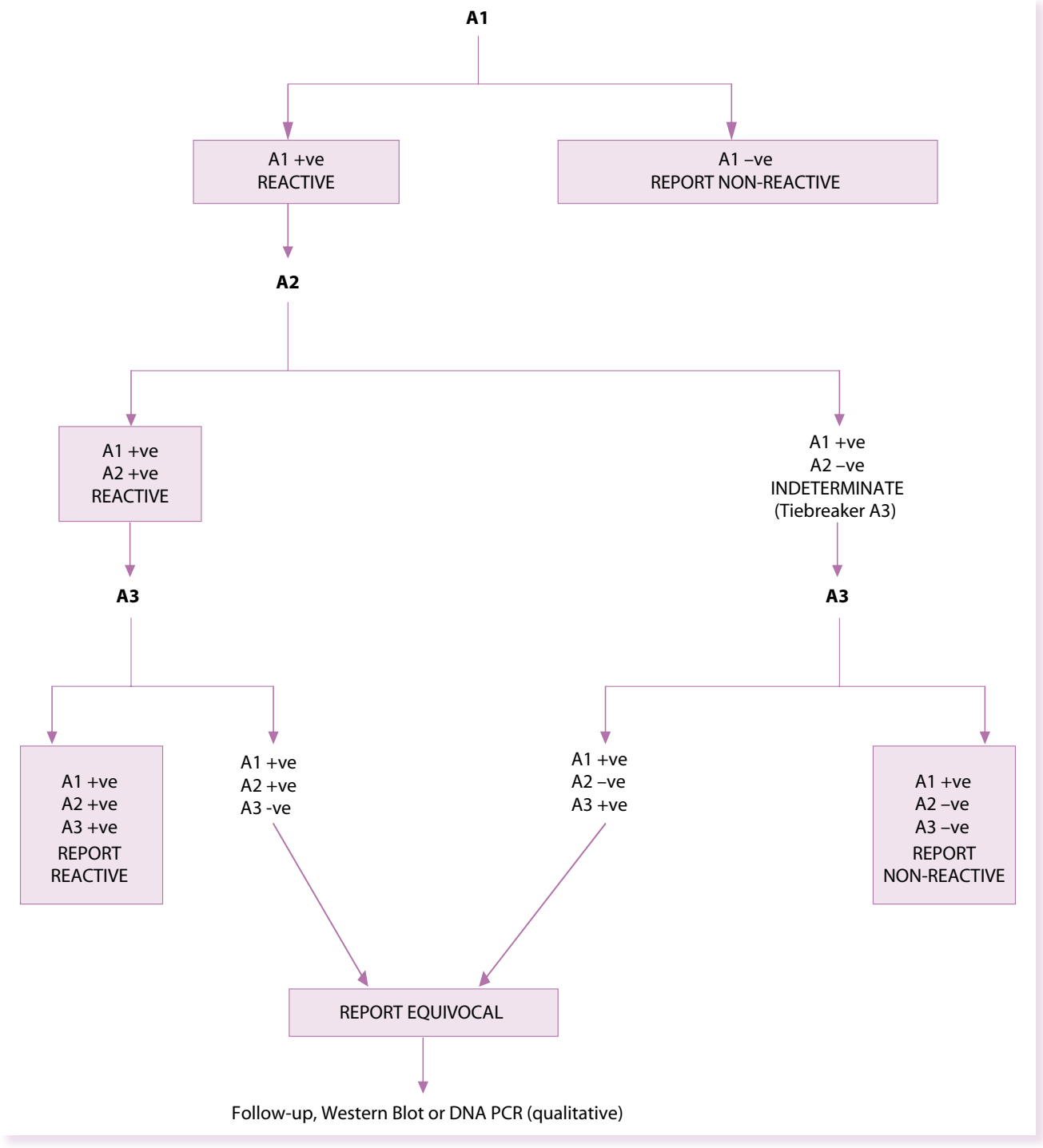
For symptomatic persons:

1.1.1 HIV testing strategy II B (Blood/Plasma/Serum)



For asymptomatic persons:

1.1.2 HIV testing strategy III



A2 Section

Assessment of Adults and Adolescents with HIV Infection and Pre-ART Care and Follow-up

2.1 Clinical Assessment

At the beginning of HIV care and prior to starting ART, a clinical assessment should be performed to:

- Determine the clinical stage of HIV infection
- Identify history of past illnesses (especially those related to HIV)
- Identify current HIV-related illnesses that require treatment
- Determine the need for ART and OI prophylaxis
- Identify coexisting medical conditions and treatments that may influence the choice of therapy

The recognition of HIV-related clinical events helps to determine the stage of a patient's disease and decisions on when to initiate OI prophylaxis and ART.

WHO stage 1, 2 and 3 conditions, with the exception of moderate anaemia, can be readily recognized clinically. For WHO stage 4 conditions, where clinical diagnosis is not possible, definite diagnostic criteria are recommended in the case of conditions such as lymphoma and cervical cancer (*See Table 1*).

2.2 Medical History

Many individuals with HIV infection may have concurrent risk behaviours. It is important to elicit these risk factors, which may influence how a person will be counselled and supported. These risk factors for HIV infection include:

- Past or present use of injecting drugs
- Male or female sex worker
- Men who have sex with men (MSM)
- Present or past unprotected sex, in particular with female or male sex worker
- Past or present sexually transmitted infection (STI)
- Past or present recipient of blood or blood products
- Injections, tattoos, ear piercing or body piercing using non-sterile instruments

See Table 2 (p11)

Table 1: WHO clinical staging of HIV/AIDS for adults and adolescents, 2006

Clinical stage 1

Asymptomatic
Persistent generalized lymphadenopathy

Clinical stage 2

Unexplained moderate weight loss (<10% of presumed or measured body weight)[1]
Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)
Herpes zoster
Angular cheilitis
Recurrent oral ulceration
Papular pruritic eruptions
Seborrhoeic dermatitis
Fungal nail infections

Clinical stage 3

Unexplained[2] severe weight loss (>10% of presumed or measured body weight)
Unexplained chronic diarrhoea for longer than one month
Unexplained persistent fever (above 37.5°C intermittent or constant for longer than one month)
Persistent oral candidiasis
Oral hairy leukoplakia
Pulmonary tuberculosis
Severe bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)
Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
Unexplained anaemia (<8 g/dl), neutropenia (<0.5 X 10^9/litre) and or chronic thrombocytopenia (<50 X 10^9/litre[3])

Clinical stage 4[3]

HIV wasting syndrome
Pneumocystis pneumonia
Recurrent severe bacterial pneumonia
Chronic herpes simplex infection (orolabial, genital or anorectal of more than one 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)
Central nervous system toxoplasmosis
HIV encephalopathy
Extrapulmonary cryptococcosis including meningitis
Disseminated non-tuberculous mycobacteria infection
Progressive multifocal leukoencephalopathy
Chronic cryptosporidiosis
Chronic isosporiasis
Disseminated mycosis (extrapulmonary histoplasmosis, coccidiomycosis)
Recurrent septicaemia (including non-typhoidal salmonella)
Lymphoma (cerebral or B cell non-Hodgkin)
Invasive cervical carcinoma
Atypical disseminated leishmaniasis
Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy

[1] Assessment of body weight in pregnant woman needs to consider expected weight gain of pregnancy.
[2] Unexplained refers to where the condition is not explained by other conditions.
[3] Some additional specific conditions can also be included in regional classifications (e.g. reactivation of American trypanosomiasis (meningoencephalitis and/or myocarditis) in Americas region, Penicilliosis in Asia).

Table 2: Medical history checklist

HIV testing	HIV risks (can have multiple factors)
• Ever tested for HIV in the past? • Date and place of first HIV test • Reason for the test • Documentation of the result • Date of last negative HIV test result • Previous CD4 cell counts (if available) • Previous viral load (if available)	• Unprotected sexual contact • Injecting drug use • Men having sex with men • Occupational exposure • Perinatal transmission • Recipient of blood products • Unknown • Partner's HIV status being positive
System review	**Past history of HIV-related illnesses**
• Unexplained weight loss • Swollen lymph nodes • Night sweats and fever • Unusual headaches or poor concentration • Changes in appetite • Skin rashes • Sores or white spots in mouth • Painful swallowing • Chest pain, cough or shortness of breath • Stomach pain, vomiting or diarrhoea • Numbness or tingling in hands or feet • Muscular weakness and changes in vision	• Oral candidiasis or candida oesophagitis • Persistent diarrhoea • Tuberculosis • Varicella zoster (shingles) • Oral hairy leukoplakia • *Pneumocystis jiroveci* pneumonia (PCP) • Recurrent bacterial pneumonia • Cryptococcal meningitis • Toxoplasmosis • Kaposi sarcoma • Disseminated *Mycobacterium avium* complex Cytomegalovirus (CMV) infection • Invasive cervical cancer
Tuberculosis history	**Sexually transmitted infections (STIs)**
• Last chest X-ray • History of past TB • Treatment given (drugs and duration) • History of exposure to TB	• Genital ulcer or other lesion • Genital discharge (abnormal vaginal discharge in women) • Lower abdominal pain
Gynaecological history	**General medical history**
• Last PAP smear • Menstrual irregularities • Pelvic pain or discharge	• Any other past medical condition, such as diabetes, hypertension, coronary artery disease,hepatitis B, hepatitis C, hyperlipidaemia • Mental health issues, e.g. depression
Pregnancy and contraception history	**Vaccination history**
• Previous pregnancies and terminations • Children and HIV status of children (living and dead) • Exposure to ARVs during pregnancy • Drugs and duration of ART • Contraception used • Last menstrual period	• BCG • Hepatitis A vaccine • Hepatitis B vaccine
Medication	**Allergies**
• Past use of drugs and reasons for taking them • Current use of drugs and reasons for taking them • Current use of traditional/herbal remedies • Opioid substitution therapy (OST)	• Known allergies to drugs or other substances or materials
ART history	**Psychosocial history**
• Current and past exposure to ARVs • ARV use during pregnancy for PMTCT • Which drugs taken and for how long	• Family history, e.g. other immediate family members with known HIV infection • Social history, e.g. marital status, education, occupation, source of income

Table 2: Medical history checklist	
Substance use	**Functional status**
• Understanding of and readiness to commence ART • Partner's ART history (if HIV-positive)	• Financial and family support status • Disclosure status, readiness to disclose • Availability of care and treatment supporter
• Alcohol, stimulant, opiate and other drug use • Smoking history	• Able to work, go to school, do housework • Ambulatory but not able to work • Bed-ridden • Amount of day-to-day care needed

2.3 Physical Examination

It is essential to have a thorough physical examination for clinical staging and screening. Table 3 details the specific physical signs related to HIV/AIDS which should be screened.

Table 3: Physical examination checklist	
Record vital signs, body weight, height and body mass index (BMI), temperature, blood pressure, pulse rate, respiratory rate	
Appearance	• Unexplained moderate or severe weight loss, HIV wasting • Rapid weight loss is suggestive of active OI, especially if associated with fever • Gradual weight loss (not caused by malnutrition or other obvious illness) is suggestive of HIV infection • "Track marks" and soft tissue infections which are common among IDUs
Consider conditions other than HIV	• Malaria, tuberculosis, syphilis, gastrointestinal infections, bacterial pneumonia, pelvic inflammatory disease, viral hepatitis
Skin	• Look for signs of HIV-related and other skin problems. These include diffuse dry skin, typical lesions of PPE, especially on the legs, seborrhoeic dermatitis on face and scalp • Look for herpes simplex and herpes zoster or scarring of previous herpes zoster (especially multi-dermatome)
Lymph nodes	• Start with posterior cervical nodes • PGL (persistent glandular lymphadenopathy) typically presents as multiple bilateral, soft, non-tender, mobile cervical nodes. Similar nodes may be found in the armpits and groins • Tuberculous lymph nodes typically present as unilateral, painful, hard, enlarging nodes, with constitutional symptoms such as fever, night sweats and weight loss
Mouth	• Look for signs suggestive of HIV infection including white plaques on tongue, cheeks and roof of mouth (oral candida), white stripped lesions on the side of the tongue (OHL) and cracking at the corners of the mouth (angular cheilitis) • Difficulty in swallowing is commonly caused by oesophageal candida
Chest	• The most common problems will be PCP and TB • Signs and symptoms are cough, shortness of breath, haemoptysis, weight loss, fever, congestion or consolidation • Perform a chest X-ray, if symptomatic
Abdomen	• Hepatosplenomegaly, masses and local tenderness • Jaundice may indicate viral hepatitis
Ano-genital	• Herpes simplex and other genital sores/lesions, vaginal or penile discharge • Perform PAP smear, if possible
Neurological examination	• Focus on visual fields and the signs of neuropathy (bilateral peripheral or localized mono-neuropathies) • Assess focal neurological deficit
Note: During each consultation, patient is to be clinically screened for TB (history and physical examination).	

2.4 Comprehensive Laboratory Evaluation in HIV/AIDS

The purpose of the baseline laboratory evaluation is to (i) determine the stage of the disease, (ii) rule out concomitant infections and (iii) determine baseline safety parameters. The following tests are part of the recommended tests for monitoring of PLHAs on treatment (*See also table 18)*.

Table 4: Rationale of laboratory evaluations in HIV/AIDS

Essential	Optional
Confirm HIV infection: HIV status must be documented. Refer to ICTC if in doubt	**Fasting lipid profile:** May be recommended in patients with established coronary disease risk factors, or if stavudine, efavirenz, protease inhibitor (PI) use is contemplated
Specific investigations: To rule out OIs, depending on the clinical need	**Pregnancy test:** EFV is contraindicated in pregnancy during the first trimester of pregnancy
CD4 counts: All patients should have a baseline screening. *(See table 6)*	**Anti-HCV screening**: The prevalence of hepatitis C virus (HCV) is low in HIV-infected patients, except, for example, in the northeastern states of India, where injecting drug use is a risk factor. Such screening is also recommended in HIV-infected haemophiliacs and thalassaemics
CBC: Hb, TLC, DLC, ESR, GBP	**Chest X-ray:** To rule out TB or other pulmonary infection based an symptoms
LFTs: Necessary to find evidence of hepatitis, particularly when NVP use is contemplated	**Plasma viral load (PVL):** A baseline PVL is not necessary. With optimum adherence and a potent regimen, undetectable levels should be achieved at 6 months after ART initiation
Urine routine: To evaluate proteinuria and sugar (may necessitate estimation of blood glucose)	
HBsAg: To rule out concomitant hepatitis B infection as this can influence choice of ARV regimen. The abrupt stopping of anti-HBV drugs such as lamivudine and tenofovir is not recommended in patients with chronic hepatitis B co-infection since it may result in hepatitis B flare-up. This screening is mandatory for IDUs and those with transfusion-associated HIV infection	
HCV screening: Mandatory for IDUs and those with transfusion-associated HIV infection	
VDRL/TPHA (syphilis screening): Especially for persons from high-risk behaviour groups, those with history of STIs and/or symptoms suggestive of syphilis	
Pap smear: Helps in earlier diagnosis of cervical intraepithelial neoplasia (CIN). Or Trichloroacetic acid staining at district facilities where Pap smear is not available	

2.5 Revised WHO Clinical Staging of HIV Disease for Adults and Adolescents, 2006

See Table 1, page 10

The revised 2006 WHO Clinical Staging are designed to be used in patients with confirmed HIV infection. When the facilities for testing CD4 count are not immediately available, the clinical staging system is used to guide decisions on when to start OI prophylaxis and when to initiate and switch ART. The schedule below includes a general timeline for patient visits, including those for assessment and management after the diagnosis of HIV has been confirmed.

Table 5: Assessment and initial management after HIV diagnosis is confirmed

Visit 1	** Refer to Table 13: Initiation of ART based on CD4 and WHO clinical staging* • Medical history • Symptom checklist • Screen for TB • Physical examination • Chest X-ray if chest symptoms present • Behavioural/psychosocial assessment: – Educational level, employment history, financial resources – Social support, family/household structure • Disclosure status, readiness to disclose • Understanding of HIV/AIDS, transmission, risk reduction, treatment options • Nutritional assessment • Family/household assessment to determine if there are other HIV-infected family members who may need care • Recommend condom use during every visit • Investigation: baseline Blood profile, CD4 count, other test as necessary	
	Eligible for ART	**Not eligible for ART**
Visit 2 (Any time)	• History (new problems) • Symptom check-list • Screen for TB • Physical examination • Co-trimoxazole prophylaxis • Psychosocial support • Adherence counselling (more than one session may be needed before commencing ART)	• History (new problems) • Symptom check-list • Physical examination • Psychosocial support
Visit 3 (2 weeks after previous visit)	• Screen for TB • Commence ART if stable on Co-trimoxazole and patient is ready • Commence lead in dose of NVP 200 mg once daily	
Visit 4 (2 weeks after previous visit)	• History (new problems) and clinical examination • Screen for TB • If on NVP, note any side-effects (rash, fever, signs of liver toxicity) • Dose escalation of NVP to 200 mg 2 times a day • Adherence assessment/support	
Subsequent visits (4 weeks after previous visit, or as necessary)	• History (new problems) • Symptom check-list • Screen for TB • Clinical examination • Adherence assessment/support	Follow-up visit for CD4 monitoring *(see Table 6)* History (new problems) Screen for TB during each visit
See table 18 (p 25) for routine monitoring after ART has been initiated.		

2.6 Pre-ART Care

With the scaling up of treatment nationally, as well as increased awareness of HIV and access to counselling and testing services, it is envisioned that there would be a decrease in the number of PLHA requiring ART as many more would present in the earlier stages of the infection. The recent experience of ART centres has shown that there is a need to emphasize good HIV (pre-ART) care and support so as to maintain well-being.

Pre-ART care is defined as the ***period where an HIV positive person does not medically require the initiation of ART.*** PLHA who do not need ART (or are not medically eligible for the initiation of ART) should be counselled to maintain healthy/positive living and be linked to care and support services. The following steps are recommended for monitoring patients who are not yet eligible for ART for the early detection of OIs and initiation of ART before the CD4 count falls below 200 cells.

- Comprehensive medical history and physical examination (*see Tables 2,3,4*)
- Baseline laboratory tests for pre-ART care patients include:
  - Baseline screening of CD4 to determine eligibility for starting ART (*see Table 13*)
  - Baseline laboratory assessment, including CBC, ALT/AST, ALP, urinalysis
  - For women: Annual PAP smear screening or acetic acid cervical screening at district health care facilities
  - HBsAg and HCV screening for IDUs/those with transfusion-associated infections or elevated liver enzyme levels
  - Any other relevant investigations (symptom-driven) and screening for TB at every visit
- Follow-up visit for pre-ART care and CD4 screening
- Educate patient to return to ART centre if unwell or new symptoms arise
- Other services for pre-ART care patients including family screening and testing/counselling of partners (couple counselling) and children, as well as follow-up of discordant couples and referral for care and support services
- Register patients in the NACO Pre-ART Register

Table 6: CD4 monitoring and follow-up schedule

CD4 count	Repeat at
< 350 and not on ART	3 months
> 350 and not on ART	6 months
on ART(any value)	6 months
> 500	Annual screening

Note: If the CD4 count is between 200 to 250 cells/mm^3 and the patient is not on ART; repeat CD4 assessment after 4 weeks and consider treatment in asymptomatic patients. *See Table 13 for more details p19.*

A3 Section

Prophylaxis of Opportunistic Infections

3.1 Co-trimoxazole Prophylaxis (CPT)

Routine prophylaxis with co-trimoxazole is provided under the national programme. CPT is efficacious against several organisms, including *Toxoplasma*, PCP and several organisms causing diarrhoea in HIV-infected persons. Recent evidence has shown that CPT helps prevent morbidity and mortality in adults with both early and advanced HIV disease.

Under the national programme, CPT may be initiated in the following scenarios:

- If CD4 is not available (or result pending): WHO clinical stage 3 and 4
- If CD4 is available: HIV infected adults with CD4 <200 cells/mm^3 *or*
  CD4 <350 cells/mm^3 and if patient is symptomatic *or*
  WHO clinical stage 3 or 4 irrespective of CD4.

It is currently recommended that prophylaxis for OI be given as per the schedule below.

Table 7: Co-trimoxazole prophylaxis recommendations, 2006

Commencing primary CPT	**CD4 not available**	**CD4 available**
	WHO clinical stage 3 or 4 (This includes all patients with TB)	Any WHO clinical stage and **CD4 <200 cells/mm^3** *or* Any WHO clinical stage, **CD4 <350 cells/mm^3** and if patient is symptomatic *or* WHO stage 3 or 4 irrespective of CD4 count
Commencing secondary CPT	For all patients who have completed successful treatment for PCP until CD4 is >200	
Timing the initiation of co-trimoxazole in relation to initiating ART	Start co-trimoxazole prophylaxis first. Start ART about two weeks later if the patient can tolerate co-trimoxazole and has no symptoms of allergy (rash, hepatotoxicity) Meanwhile, make use of the time for adherence and treatment preparation	
Dosage of cotrimoxazole in adults and adolescents	One double-strength tablet or two single-strength tablets once daily– total daily dose of 960 mg (800 mg SMZ + 160 mg TMP)	
Cotrimoxazole for pregnant women	Women who fulfil the criteria for CPT should continue on it throughout pregnancy. If a woman requires CPT during pregnancy, it should be started regardless of the stage of pregnancy Breastfeeding women should continue CPT where indicated	
Patients allergic to sulpha-based medications	Dapsone 100 mg per day, if available Co-trimoxazole desensitization may be attempted but not in patients with a previous severe reaction to CTX or other sulpha-containing drugs	
Monitoring	No specific laboratory monitoring is required in patents receiving co-trimoxazole	

Note: NACO provides CD4 assessment free of cost to all patients as per medical eligibility.

Table 8: When to stop co-trimoxazole prophylaxis		
When to stop prophylaxis (co-trimoxazole or dapsone) in patients on ART	**CD4 count not available**	**CD4 count available**
	Continue prophylaxis indefinitely until CD4 count can be taken	If CD4 count >200 for at least 6 months ***and*** If patient is on ART for at least 6 months, is asymptomatic and well

Notes:

* If CPT is started at CD4 levels between 200–350 cells/mm^3: CD4 counts should have increased, patient is on ART for at least 6 months, is asymptomatic and well; before CPT is stopped.

Some OIs may require secondary prophylaxis as detailed in table 9.

Table 9: Recommended schedule for starting and stopping OI prophylaxis				
Opportunistic infection	**Primary prophylaxis indicated when CD4 is**	**Drug of choice**	**Discontinue primary prophylaxis when CD4 is**	**Discontinue secondary prophylaxis when CD4 is**
PCP	< 200	TMP-SMX 1 DS od	>200	
Toxoplasmosis	< 100	TMP-SMX 1 DS od	>200	
CMV retinitis	Not indicated	Secondary: oral ganciclovir	Not applicable	>100
Cryptococcus meningitis	Not indicated	Secondary: fluconazole	Not applicable	>100
Oral and oesophageal candidiasis	Not indicated	Not applicable	Not applicable	Not indicated

Note:

- Start co-trimozaxole when CD4 count is less than 200 or WHO Clinical Stage 3 or 4, irrespective of CD4. This includes all HIV-TB co-infected patients
- Discontinue when two consecutive CD4 counts are more than the respective levels, the patient is on ART more than 6 months and adherence is good
- Reintroduce prophylaxis if CD4 count falls below 200 again
- Secondary prophylaxis is indicated to prevent recurrent OI

3.2 Co-trimoxazole desensitization

If the patient reports a history of hypersensitivity to sulpha-containing drugs, start him/her on a desensitization regimen as an in-patient. Desensitization can be attempted two weeks after a non-severe (grade 3 or less) co-trimoxazole reaction which has resulted in a temporary interruption in the use of the drug.

Co-trimoxazole desensitization has been shown to be successful and safe in approximately 70% of patients with previous mild to moderate hypersensitivity.[1,2,3] Desensitization should not be attempted in individuals with a history of severe co-trimoxazole or other sulphonamide reaction. If a reaction occurs, the desensitization regimen should be stopped. Once the patient recovers fully, dapsone at a dosage of 100 mg per day may be tried. Some patients may be allergic to both co-trimoxazole and dapsone. There are no other prophylaxis drug options in resource-limited settings.

Table 10: Protocol for co-trimoxazole desensitization		
Step	**Dosage**	
Day 1	80 mg SMX + 16 mg TMP	(2 ml oral suspension)
Day 2	160 mg SMX + 32 mg TMP	(4 ml oral suspension)
Day 3	240 mg SMX + 48 mg TMP	(6 ml oral suspension)
Day 4	320 mg SMX + 64 mg TMP	(8 ml oral suspension)
Day 5	One single-strength SMX-TMP tablet	(400 mg SMX + 80 mg TMP)
Day 6	Two single-strength SMX-TMP tablets or one double-strength tablet	(800 mg SMZ + 160 mg TMP)

Reference: *Guidelines on co-trimoxazole prophylaxis for HIV-related infections among children, adolescents and adults in resource-limited settings: Recommendations for a public health approach. World Health Organization, 2006.*

Note: Co-trimoxazole oral suspension contains 40 mg TMP + 200 mg SMX per 5 ml

A4 Section

ART in Adults and Adolescents

4.1 ARV Drugs: Action and Use

Antiretroviral agents are drugs which act at various stages of the life cycle of HIV in the body and work by interrupting the process of viral replication. Theoretically, ARV drugs can act in any of the following ways during different stages of viral replication:

(i) Block binding of HIV to target cell (*fusion inhibitors*)

(ii) Block viral RNA cleavage and one that inhibits reverse transcriptase (*reverse transcriptase inhibitors*)

(iii) Block the enzyme, integrase, which helps in the incorporation of the proviral DNA into the host cell chromosome (*integrase inhibitors*)

(iv) Block the RNA to prevent viral protein production

(v) Block the enzyme protease (*protease inhibitors*)

(vi) Inhibit the budding of virus from host cells

The currently available agents target the virus mainly by inhibiting the enzymes reverse transcriptase (RT inhibitors) and protease (protease inhibitors), and preventing fusion of the virus with CD4 cells (fusion inhibitors). New classes of drugs are emerging.

Table 11: Classes of drugs available

Nucleoside reverse transcriptase inhibitors (NRTI)	Non-nucleoside reverse transcriptase inhibitors (NNRTI)	Protease inhibitors (PI)
Zidovudine (AZT/ZDV)*	Nevirapine* (NVP)	Saquinavir* (SQV)
Stavudine (d4T)*	Efavirenz*(EFV)	Ritonavir* (RTV)
Lamivudine (3TC)*	Delavirdine (DLV)	Nelfinavir* (NFV)
Didanosine (ddI)*		Amprenavir (APV)
Zalcitabine (ddC)*	**Fusion inhibitors (FI)**	Indinavir* (INV)
Abacavir (ABC)*	Enfuviritide (T-20)	Lopinavir/Ritonavir (LPV)*
Emtricitabine (FTC)		Foseamprenavir (FPV)
(NtRTI)	**Integrase Inhibitors (new)**	Atazanavir (ATV)*
Tenofavir (TDF)*		Tipranavir (TPV)
	CCR5 Entry Inhibitor (new)	

* Available in India

4.2 Goals of Antiretroviral Therapy

The currently available ARV drugs cannot eradicate the HIV infection 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 as follows.

Table 12: Goals of ARV therapy
• **Clinical goals:** Prolongation of life and improvement in quality of life
• **Virological goals:** Greatest possible reduction in viral load for as long as possible
• **Immunological goals:** Immune reconstitution that is both quantitative and qualitative
• **Therapeutic goals:** Rational sequencing of drugs in a fashion that achieves clinical, virological and immunological goals while maintaining treatment options, limiting drug toxicity and facilitating adherence
• **Reduction of HIV transmission in individuals:** Reduction of HIV transmission by suppression of viral load

In general, the clinical management of an HIV patient revolves around optimizing the treatment regimen, reducing drug toxicity, reducing the pill burden and increasing adherence to the treatment.

4.3 When to start ART in Adults and Adolescents

4.3.1. All persons registered for care and treatment at ART centres should have their full history taken and undergo clinical examination, including determining the clinical stage of HIV (*see Table 1*). The initiation of ART is based on the clinical stage and the CD4 count is used to guide treatment and follow-up. **The lack of a CD4 result should not delay the initiation of ART if the patient is clinically eligible according to the WHO clinical staging, but a CD4 test should be done as soon as possible.**

4.3.2 All HIV-positive persons are eligible for CD4 testing for the purpose of screening for ART eligibility, under the national programme. Priority is given to the following groups.

- All HIV-positive persons in WHO clinical stages 3 and 4
- All persons tested HIV positive 6–8 years ago
- PLHA with a history of pulmonary TB and/or herpes zoster
- If the CD4 count assessed by a private laboratory is less than 350 cells/mm^3
- HIV-infected partners of AIDS patients
- All pregnant HIV-positive women
- All HIV-positive children (<15 years of age)

Table 13: Initiation of ART based on CD4 count and WHO clinical staging

Classification of HIV-associated clinical disease	WHO clinical stage	CD4 test not available (or result pending)	CD4 test available
Asymptomatic	**1**	Do not treat	Treat if CD4 <200
Mild symptoms	**2**	Do not treat	
Advanced symptoms	**3**	Treat	Consider treatment if CD4 <350 and initiate ART before CD4 drops below 200
Severe/advanced symptoms	**4**	Treat	Treat irrespective of CD4 count

Notes:

- Determining the clinical stage is part of the baseline assessment (first visit) on entry into the care and treatment programme. Clinical staging is used to guide decisions on initiating co-trimoxazole prophylaxis and ART when CD4 testing facilities are not immediately available (or the result is pending).

- Offer ART to symptomatic patients if the CD4 count is 200–350 cells/mm^3.
- Consider ART for asymptomatic patients with CD4 count between 200-350 cells/mm^3 and monitor closely for new symptoms.
- If the CD4 count is 200–250 cells/mm^3, physicians can consider repeating the CD4 test in 4 weeks in asymptomatic patients. This is to rule out the possibility of a 20% margin of error in laboratory results.
- Patients should start ART before the CD4 count drops below 200 cells/mm^3.

Starting ART by using CD4 guidance: The optimum time to start ART is before the patient becomes unwell or presents with the first OI. The progression of the disease is faster in patients who commence ART when the CD4 count falls below 200 cells/mm^3 than in those who start ART before the count drops to this level. **Patients should start ART before the CD4 count drops below 200 cells/mm^3.**

The CD4 count should be assessed after stabilization of any concurrent illness because the absolute CD4 count can vary with illness. The CD4 count should be used as a *supplement to clinical assessment* for determining the stage of the disease in matters of decision-making. **All HIV-confirmed persons should be referred to ART centres for registration into care and screening for medical eligibility for ART.**

Do NOT delay ART initiation if the patient is clinically eligible according to the WHO Clinical Staging criteria, in absence of a CD4 count

4.3.3 The total lymphocyte count is no longer used in the national ART programme as global evidence has shown that TLC is a poor parameter for deciding on the initiation of ART, especially in asymptomatic persons, and monitoring the response to ART.

4.3.4 Ensuring good adherence to the treatment is imperative for the success of the national programme as well as for the prevention of drug resistance. To achieve this, counselling must start from the first contact visit by the clinical team and should include preparing the patient for treatment and providing psychosocial support through an identified guardian/treatment buddy and through support networks. All patients should undergo **at least two counselling sessions** before the initiation of ART. The period of investigations should be utilized for counselling and treatment preparation. All efforts should be made to trace patients who have defaulted or are lost to follow-up. NGO and positive network linkages should be established by each ART centre for the respective locality.

4.4 Manage OIs Before Starting ART

4.4.1 Commencing ART in the presence of active OIs

Do not start ART in the presence of an active OI. In general, OIs should be treated or stabilized before commencing ART. *Mycobacterium Avium Complex* (MAC) and progressive multifocal leukoencephalopathy (PML) are exceptions, in which commencing ART may be the preferred treatment, especially when specific MAC therapy is not available. For details on starting ART in patients with HIV-TB co-infection, see the section on the management of HIV-TB. Some conditions which may regress following the commencement of ART include candidiasis and cryptosporidiosis.

The following OIs and HIV-related illnesses need treatment or stabilization before commencing ART.

Table 14: Managing OIs before starting ART

Clinical picture	Action
Any undiagnosed active infection with fever	Diagnose and treat first; start ART when stable
TB	Treat TB first; start ART as recommended in TB section (P 30)
PCP	Treat PCP first; start ART when PCP treatment is completed

Table 14: Managing OIs before starting ART	
Invasive fungal diseases: oesophageal candidiasis, cryptococcal meningitis, penicilliosis, histoplasmosis	Treat esophageal candidiasis first; start ART as soon as the patient can swallow comfortably Treat cryptococcal meningitis, penicilliosis, histoplasmosis first; start ART when patient is stabilized or OI treatment is completed
Bacterial pneumonia	Treat pneumonia first; start ART when treatment is completed
Malaria	Treat malaria first; start ART when treatment is completed
Drug reaction	Do not start ART during an acute reaction
Acute diarrhoea which may reduce absorption of ART	Diagnose and treat first; start ART when diarrhoea is stabilized or controlled
Non-severe anaemia (Hb < 8 g/litre)	Start ART if no other causes for anaemia are found (HIV is often the cause of anaemia); avoid AZT
Skin conditions such as PPE and seborrhoeic dermatitis, psoriasis, HIV-related exfoliative dermatitis	Start ART (ART may resolve these problems)
Suspected MAC, cryptosporidiosis and microsporidiosis	Start ART (ART may resolve these problems)
Cytomegalovirus infection	Treat if drugs available; if not, start ART
Toxoplasmosis	Treat; start ART after 6 weeks of treatment and when patient is stabilized

4.5 Antiretroviral Therapy Regimens

4.5.1 Currently, the national programme provides the following combinations for first-line regimens

(i) Stavudine (30 mg) + Lamivudine (150 mg)

(ii) Zidovudine (300 mg) + Lamivudine (150 mg)

(iii) Stavudine (30 mg) + Lamivudine (150 mg) + Nevirapine (200 mg)

(iv) Zidovudine (300 mg) + Lamivudine (150 mg) + Nevirapine (200 mg)

(v) Efavirenz (600 mg)

(vi) Nevirapine (200 mg)

Fixed-dose combinations (FDCs) are preferred because they are easy to use, have distribution advantages (procurement and stock management), improve adherence to treatment and thus reduce the chances of development of drug resistance. The current national experience shows that bid (twice a day) regimens of FDCs are well tolerated and complied with. At present, second-line drug regimens are not available under the national programme.

4.5.2 Recommended choices of first-line regimens

Principles for selecting the first-line regimen

1. Choose 3TC (lamivudine) in all regimens
2. Choose one NRTI to combine with 3TC (AZT **or** d4T)
3. Choose one NNRTI (NVP **or** EFV)

First choice: AZT + 3TC + NVP (for patients with Hb > 8 g/dl)

Second choice: d4T + 3TC + NVP

} Substitute NVP with EFV, for patients with TB or toxicity to NVP

4.5.3 Special considerations

- TDF + 3TC + (NVP or EFV): This combination is only for special situations, for example, when there is toxicity or other contraindications to AZT or d4T. Substituted with TDF.
- AZT + 3TC + TDF[4]: This is for individuals who are unable to tolerate NVP or EFV.

These special combinations using TDF are provided on a case-to-case basis and decided upon by an expert panel at the State AIDS Control Society (SACS). The panel consists of two physicians with experience in ART, one representative from SACS and one from the positive network.

Table 15: Recommended first-line antiretroviral regimens

Recommendation	Regimen	Comments
Preferred first-line regimen	AZT + 3TC + NVP	AZT may cause anaemia, which requires Hb monitoring, but is preferred over d4T because of d4T toxicity (lipoatrophy, lactic acidosis, peripheral neuropathy) Patients who develop severe anaemia while on an AZT-based regimen should not be re-challenged with AZT. In such cases, the patient should receive either d4T or TDF in place of AZT For women with CD4 > 250 cells/mm^3, monitor for hepatotoxicity closely if started on the NVP-based regimen
Alternative first -line regimens	AZT + 3TC + EFV	EFV is substituted for NVP in cases of intolerance to the latter or if patients are receiving rifampicin-containing anti-TB treatment EFV should not be used in patients with grade 4 or higher elevations of ALT
	D4T + 3TC + (NVP or EFV)	If the patients have anaemia, a d4T-based regimen should be prescribed
Other options	TDF + 3TC + (NVP or EFV) *or* AZT + 3TC + TDF	TDF is supplied on a case-to-case basis by SACS after evaluation by the SACS clinical expert panel

Table 16: Choice of NRTIs

NRTI	Advantages	Disadvantages
3TC	Good safety profile, non-teratogenic Once daily Effective against hepatitis B Widely available, including in FDCs	Low genetic barrier to resistance
FTC **	An alternative to 3TC Good safety profile Same efficacy as 3TC against HIV and hepatitis B and the same resistance profile	No added advantage over 3TC except as daily dose Can be used as once-a-day dose in combination with TDF and EFV. (i.e. reduced pill burden and dosing schedule)
TDF *	Good efficacy, safety profile Once daily regimens Metabolic complications, such as lactic acidosis and lipoatrophy, are less common than with d4T	Renal dysfunction has been reported Safety in pregnancy not established Adverse effects on foetal growth and bone density reported Limited availability at SACS on case-to-case basis

AZT	Generally well tolerated Widely available, including in FDCs Metabolic complications less common than with d4T	Initial headache and nausea Severe anaemia and neutropenia Haemoglobin monitoring recommended
ABC **	Good efficacy profile Once daily Causes the least lipodystrophy and lactic acidosis	Severe hypersensitivity reaction in 2–5% of adults
D4T	Good efficacy profile and cheap No or limited laboratory monitoring Widely available in FDCs	Most associated with lactic acidosis, lipoatrophy and peripheral neuropathy

* Shall be available on case-to-case basis
** Not supplied by NACO at present

4.5.4 Recommendations on stavudine (d4T) 30mg

(based on the WHO 2007 April amendment)

Previously, the preferred d4T dosing was weight-based. Dosing for patients >60 kg was recommended at 40 mg twice daily; dosing for patients <60 kg was recommended at 30 mg twice daily.

Based on review of available evidence, WHO recommends that 30 mg formulation of stavudine, dosed twice daily, should be used irrespective of the patient's body weight in adults and adolescents. This recommendation is now the preferred dose when d4T is used as part of an ARV therapeutic regimen:

- All new patients with weight over 60 kg being prescribed d4T should be started on d4T30 mg. No patients already receiving d4T 30 mg should be stepped up to d4T 40 mg.
- All patients receiving d4T 40 mg should be moved to d4T 30mg as soon as possible, even without evidence of stavudine toxicity.

Table 17: Starting an NVP-based regimen

Starting nevirapine –based regimen		
	Morning	**Evening**
Lead-in NVP dose for the first 2 weeks	FDC (AZT or d4T + 3TC) one pill + NVP one pill	FDC (AZT or d4T +3TC) one pill No NVP
Escalate to full NVP dose after 2 weeks	FDC (AZT or d4T + 3TC + NVP) one pill	FDC (AZT or d4T + 3TC + NVP) one pill

4.5.5 **The lead-in period for NVP dosing** at 200 mg once daily for the first two weeks produces adequate NVP levels. Due to enzyme auto-induction, NVP levels decline over two weeks and an increase in the dosage to 200 bid is required to maintain adequate levels. Starting with the full NVP dosage without a lead-in period results in a very high serum concentration of the drug and increases the risk of hepatotoxicity and rash. If NVP is restarted after more than 14 days of treatment interruption (due to whatever reason, e.g. elevated liver enzymes), the lead-in dosing is again necessary.

PIs are not recommended in first-line regimen because their use in an initial treatment regimen essentially rules out second-line regimen options.

4.5.6 Efavirenz (EFV) should be given to the following groups of persons:

- In PLHA receiving concurrent rifamipicin-containing anti-TB regimen (ATT) for the duration of the anti-TB treatment
- In cases with clinical or laboratory evidence of hepatic dysfunction, e.g. due to hepatitis B/C co-infection or other causes
- In patients with significant NVP side-effects/toxicity and in whom NVP re-challenge cannot be done.

4.5.7 Patients on an NVP regimen who have been switched over to EFV because of rifampicin-containing anti-TB treatment should be shifted back to NVP after completion of the TB treatment[5] (unless other contraindications to NVP exist).

- The change from EFV to NVP should be made two weeks after completing the anti-TB treatment.
- In this particular scenario, the lead-in dose/period is not necessary while shifting from EFV to NVP (i.e. should start immediately on bid NVP dosage).
- Patients should be monitored closely for NVP toxicity (hepatotoxicity), particularly if the CD4 count is >250 cells/mm^3, especially in women.

4.5.8 For women of the reproductive age group, screening for pregnancy should be carried out. Testing for pregnancy is essential if EFV is being considered for use. For women who are of the child-bearing age and have been started on EFV, counselling and support on consistent contraception use is needed.

EFV is contraindicated in pregnant HIV-infected women during the first trimester of pregnancy because of concerns of teratogenicity

See Annex 2: Drug combinations and strategies not to be used

A5 Section

Routine Monitoring of Patients on ART

5.1 Follow-up and monitoring is essential in patients initiated on ART to track clinical progress and monitor wellbeing. The routine monitoring and follow-up schedule for patients on ART under the national programme is detailed in table 18.

Table 18: Monitoring and follow-up schedule for patients on ART

	Day 0 (baseline) Before or at start of ART	At 15 days	At 1 month	At 2 months	At 3 months	Every 6 months	Consultation as needed (symptom-directed)
Clinical and adherence counselling	✓	✓	✓	✓	✓	✓	
Weight	✓	✓	✓	✓	✓	✓	
Hb	✓	✓ (if on AZT)	✓ (if on AZT)		✓	✓	✓
ALT *	✓	✓ (if on NVP)	✓ (if on NVP)		✓*	✓*	✓
Random blood sugar	✓					✓ (if on PI)	
CD4	✓					✓	✓
Urinalysis	✓					✓ (if on TDF)	
Lipid profile**	✓ (only planning for PI)					✓ (if on PI)	✓**
Pregnancy test for women with reproductive potential	✓ (if planning for EFV)						✓
HBV and HCV screening	✓ (if history of IDU, transfusion-related transmission)						

Table 18: Monitoring and follow-up schedule for patients on ART

	Day 0 (baseline) Before or at start of ART	At 15 days	At 1 month	At 2 months	At 3 months	Every 6 months	Consultation as needed (symptom-directed)
VDRL/ TPHA (syphilis screening)	✓ (if history of high-risk behaviour, recurrent STIs and/or symptoms suggestive of syphilis)						
Plasma viral load* **						✓	

Notes:

* For patients co-infected with HBV and/or HCV, and on ART; three to six- monthly monitoring of liver function is recommended.

** d4T and PIs may cause lipid abnormalities. In patients with significant risk factors for coronary artery disease, a fasting lipid may be done at 6 months; otherwise annual screening is sufficient.

*** The national programme does not recommend routine viral load monitoring. Viral load measurement is not recommended for decision-making for the initiation or regular monitoring of ART in resource-limited settings (WHO 2006). It may be considered for the diagnosis of early treatment failure or to assess discordant clinical and CD4 findings in patients in whom failure of ART is suspected.

Scheduled follow-up is necessary during the initial months of ART to diagnose and manage acute adverse events efficiently, work with the patient on adherence issues, and diagnose clinical conditions like IRS and new episodes of OIs.

5.2 The estimation of the CD4 count for patients receiving ART is recommended at six months to document immunological improvement. After the initiation of an NVP-based regimen, ALT measurement is recommended in the first month to detect drug-induced hepatitis. With an AZT-based regimen, it is important to monitor CBC for the early detection of haematological toxicity. The prevalence of lipid abnormalities is significantly frequent in patients on ART, particularly if they are on d4T, EFV or PIs. In the case of such patients and those with significant risk factors for coronary artery disease, a fasting lipid profile should be done at six months. Otherwise, yearly estimations suffice. Random blood sugar is recommended as part of the baseline screening of all patients to be started on ART, as currently one of the major causes of morbidity in India is diabetes.

A6 Section

ART in Pregnant Women, PPTCT and Previous Exposure to NVP

6.1 Pregnancy is a special situation which provides a unique opportunity for the prevention of vertical transmission of HIV using various interventions. The risk of transmission of HIV from an infected mother is 14–32% if the child is not breastfed, and 25–48% if the child is breastfed. More than two-thirds of such transmission occurs during labour, when the baby is exposed to maternal genital fluids, and a significant proportion occurs through breastfeeding.

6.2 The goals of management of HIV in pregnancy are dual: managing the mother's HIV status and prevention of mother-to-child transmission (PMTCT). **The indications for ART and drug selection in pregnancy are similar to those in non-pregnant women**. However, in the selection of a drug regimen, the following points should be remembered.

- AZT should be included as one of the components of the regimen unless there are absolute contraindications for using it.
- EFV should be avoided in the first trimester of pregnancy (because of the risk of teratogenicity).
- When NVP is used and the mother's CD4 count is >250/mm^3, close monitoring of liver function is required.

When women who are already on ART become pregnant, the benefits and risks of ART in the first trimester need to be considered. The benefits are a reduction in the risk of developing resistance and a decrease in the risk to the mother. The risk of continuing ART consists of the potential for ARV fetal toxicity, particularly during the first trimester of pregnancy. Good clinical management of HIV in pregnant women requires the support of a multidisciplinary team, including antenatal specialists, paediatricians, counsellors, members of the ART centre and community-based organizations (NGOs, positive network, etc.).

6.3 **All HIV-positive women should be referred to the ART centre for registration into care and screened for medical eligibility for ART once they have been diagnosed in the PPTCT programme.** In the case of pregnant HIV-positive women, the CD4 count should be assessed as per the national guidelines. These women should be jointly managed by the ART centre for the HIV/ART aspects and the antenatal team for obstetric concerns. **Co-trimoxazole prophylaxis is indicated in HIV-positive pregnant women as per the guidelines for adults.**

6.4 The criteria for initiating ART in pregnant women are the same as for other adults.:

- WHO clinical stage 3 or 4 disease
- WHO clinical stage 1 or 2 disease and CD4 <200 cells/mm^3
- WHO stage 3 disease and CD4 <350 cells/mm^3

The initiation of ART helps prevent transmission of HIV to the newborn and also benefits the mother's own health. Once initiated, it should be continued postpartum.

Table 19: When to start ART in pregnant women		
WHO stage	**CD4 testing not available (or results pending)**	**CD4 testing available**
1	Do not treat	Treat if CD4 <200 cells/mm^3
2	Do not treat	
3	Treat	Treat if CD4 <350 cells/mm^3
4	Treat	Treat irrespective of CD4
Note: Consider initiation of ART in asymptomatic HIV-infected pregnant women with CD4 <250 cells/mm^3 and initiate before CD4 count drops below 200 cells/mm^3.		

6.5 The following are the first-line ART regimens for pregnant women requiring treatment for her own health:

- AZT + 3TC + NVP
- EFV can be used as a substitute for NVP if there are contraindications to NVP, such as hepatotoxicity and rash. EFV should be used with caution as it is associated with the risk of foetal teratogenicity during the first trimester of pregnancy. Women should be counselled thoroughly on exposure and risk; and good paediatric follow-up is essential after the delivery of the infant.

6.6 **NVP in women with CD4 count of 200–350 cells/mm3:** There are data to show that women with a CD4 count of >250 cells/mm^3 face a higher risk of severe hepatotoxicity when they are started on an NVP-based regimen. This happens most often in the first 6–12 weeks of therapy. It is recommended that such women should undergo the following:

- Close observation over the first 12 weeks of therapy (every 2 weeks).
- Baseline and regular monitoring of liver enzymes (at baseline and at 2, 4, 8 and 12 weeks, followed by symptom-directed evaluation).
- Patient education to encourage them to return if there are problems such as rash, abdominal pain, jaundice and fever.

If the liver enzymes increase to grade 3 or higher (ALT and/or AST >5.1 times the upper normal limit) without an alternative explanation, NVP should be permanently discontinued. If symptoms suggesting hepatic toxicity, including rash, develop in pregnant women, NVP should be discontinued immediately.

For those with anaemia during pregnancy, the problem should be managed by conservative methods, such as giving ferrous folate, other oral preparations and blood transfusion (if required).

The preferred NRTIs for use in pregnant women are AZT and 3TC. The combination of ddI and d4T should not be used because of associated increased toxicities in pregnant women. Studies have shown that TDF is associated with decreased foetal growth and bone demineralization.

The preferred NNRTI is NVP, with which there has been extensive clinical experience globally. Its efficacy in reducing mother-to-child transmission has been proven. SQV/r and Nelfinavir (NLF) are the preferred PIs if the woman needs to take PIs. EFV may be considered after the first trimester.

6.7 The following are some other options for the treatment of pregnant women:

- In pregnant women who are on a first-line EFV-based regimen, EFV should be substituted with NVP in the first trimester. Women with higher CD4 cell counts should be monitored closely.
- ART is recommended for postpartum breastfeeding women who meet the medical criteria for the initiation of ART for their own health. The preferred regimen is AZT + 3TC + NVP.
- Women who have previously received single-dose NVP for PPTCT should be considered eligible for the first-line NNRTI-based regimens. Alternatives may be considered for women whose exposure to single-dose NVP has been for less than six months and who require ART for their own health – **refer for expert opinion.**

6.8 Interaction between ART and Hormonal Contraception

NVP, ritonavir (RTV), nelfinavir (NLF), Lopinavir/ritonavir (LPV/r) and Saquinavir/ritonavir (SQV/r) result in reduced ethinyl oestradiol levels. Oestrogens are slightly increased by atazanavir (ATV), indinavir (IDV) and efavirenz (EFV). Thus, women on ART should not use hormonal contraception or should use it with caution and appropriate dose adjustment. They should consult a gynaecologist for expert opinion.

Studies have shown that medroxyprogresterone acetate (Depoprovera injectable) does not interact with NVP, EFV or NLF. Hence it may be considered for use as a contraceptive. Intrauterine contraceptive devices may be used with caution in HIV-infected women with close monitoring because of the risk of intrauterine infection.

The consistent use of condoms is recommended for all HIV-infected women who are on ART. This is for the prevention of secondary transmission of HIV from/to the partner, as well as the prevention of unplanned pregnancy.

For complete overview, refer to National Guidelines on PPTCT

A7 Section

Considerations for Co-infection of Tuberculosis and HIV

7.1 HIV-TB co-infection is one of the most challenging issues in the effort to scale up ART since more than 60% of PLHA develop TB. Patients with TB merit special consideration because the co-management of HIV and TB is complicated by drug interactions between rifampicin and NNRTIs and PIs; IRIS; pill burden; adherence; and drug toxicity. Active TB is the commonest OI among HIV-infected individuals and is also the leading cause of death in PLHA.

The management of patients with HIV and TB poses many challenges, including patient acceptance of both diagnoses. HIV-infected persons with TB often require ART and WHO recommends that ART be given to:

- all patients with extrapulmonary TB (stage 4), and
- all those with pulmonary TB (stage 3) unless CD4 count is >350 cells/mm^3.

ART reduces the incidence and recurrence of TB, as well as the fatality rates. Co-trimozaxole prophylaxis should be given to HIV–TB patients as per the guidelines.

7.2 When to start first-line ART in patients with active TB: If a patient with active TB is diagnosed with HIV and requires ART, the first priority is to start TB treatment in accordance with the RNTCP guidelines. ART may need to be started later, keeping in mind the pill burden, time needed for acceptance of the diagnosis, counselling needs, drug interactions, toxicity and IRIS (*see Table 20*).

Table 20: Initiation of first-line ART in relation to anti-TB therapy
(Based on 2006 WHO guidelines)

CD4 cell count (cells/mm^3)	Timing of ART in relation to initiation of TB treatment	ART recommendations
CD4 < 200	Start ATT first Start ART as soon as TB treatment is tolerated (between 2 weeks and 2 months)[i]	Recommend ART[ii] EFV-containing regimens[iii]
CD4 between 200–350	Start ATT first Start ART 8 weeks after starting ATT (i.e. after completion of TB-intensive phase)	Recommend ART[vi]
CD4 > 350	Start ATT first Re-evaluate patient for ART at 8 weeks and at end of TB treatment	Defer ART[v]
CD4 not available	Start ART 2–8 weeks after ATT initiation	Recommend ART[iv]

Notes:

i) Timing of ART initiation is based on clinical judgement, in accordance with other signs of immunodeficiency and WHO clinical stages. In the case of extrapulmonary TB, ART should be started as soon as TB treatment is tolerated, irrespective of the CD4 count.

ii) ART should be started as soon as TB treatment is tolerated, particularly in patients with severe immunosuppression.

iii) EFV-containing regimens include d4T/3TC/EFV and AZT/3TC/EFV.

iv) ART should be started if other non-TB stage 3 or 4 events are present.

v) For some types of TB that generally respond well to anti-TB therapy (i.e. lymph node TB, uncomplicated pleural effusion), or some cases where uncomplicated pulmonary TB disease is responding well to TB treatment, consider deferring ART initiation.

vi) Rationale for ART recommendation during TB treatment (References 6,7,8,9,10,11) :

- HIV-infected patients with a CD4 count of 200–350 cells/mm^3 are at an increased risk of developing active tuberculosis, even in regions with high-baseline TB prevalence
- HIV-infected patients with a CD4 count of 200–350 cells/mm^3 and active tuberculosis are at a greater risk of AIDS and death than those without TB and with CD4 counts in the same range
- In the absence of ART, TB therapy alone does not significantly increase the CD4 cell count. Nor does it significantly decrease the HIV viral load. Thus, CD4 counts measured during active TB are likely to reflect the actual level of immunosuppression
- The use of HAART in patients with TB can lead to a sustained reduction in the HIV viral load. It can also facilitate immunological reconstitution, and decrease AIDS-defining illness and mortality. This benefit is seen across different ranges of CD4 counts

7.3 The level of EFV in the blood decreases in the presence of rifampicin. Recent data has shown that increasing the EFV dose from 600 mg/day to 800 mg/day in patients weighing less than 60 kg and receiving both EFV and rifampicin is not beneficial. Further clinical studies are being conducted in this area. In the meantime, **the use of the standard 600 mg/day dose of EFV is recommended for patients receiving EFV and Rifampicin.**

7.4 IRIS may occur in up to one-third of patients who have been diagnosed with TB and who have started ART . It typically presents within three months of the initiation of ART but can occur as early as five days. Patients with TB-associated IRIS most commonly present with fever and worsening of pre-existing lymphadenopathy or respiratory disease. The symptoms are similar to the paradoxical reactions seen in immuno-competent patients on ATT, but occur more frequently. Most cases resolve without any intervention and ART can be safely continued. Serious reactions, such as tracheal compression caused by massive adenopathy or respiratory difficulty, may occur. Therapy may require the use of corticosteroids.

7.5 There are two issues to be considered if TB is diagnosed in patients already receiving ART. The first is modification of ART (*see Table 21*).

Table 21: ART recommendations for patients who develop TB within six months of starting a first-line or second-line ART regimen

First-line or second-line ART regimen	ART regimen at the time TB occurs	Management options
First-line ART	(AZT or D4T) + 3TC + EFV	Continue with two NRTIs + EFV
	(AZT or D4T)+ 3TC + NVP	Substitute NVP with EFV[i,ii] or Substitute with triple NRTI regimen
	AZT + 3TC + TDF	Continue with triple NRTI regimen
Second-line ART	Two NRTIs + PI	Substitute or continue with LPV/r - containing regimen and adjust the dose of RTV[iii]

Notes:

i) Shifting back to the original regimens once the rifampicin-containing regimen is completed is recommended. When substituting back from EFV to NVP, no lead-in dose is required.

ii) EFV should not be used in the first trimester of pregnancy. In women of child-bearing age, the use of contraceptives should be ascertained.

iii) Monitor closely for ALTs, particularly when PIs and rifampicin are being used concurrently.

The second issue is whether when a patient on ART presents with active TB, it can be said to constitute ART failure. WHO recommends the following guiding principles in this context:

- If an episode of TB occurs within the first six months of the initiation of ART, it should not be considered as failure of the treatment, and the ART regimen should be adjusted for co-administration with rifamipicin-containing regimens.
- If an episode of TB develops more than six months after the initiation of ART, and data on the CD4 count (and viral load), is available, the decision on whether the diagnosis of TB represents ART

failure should be based on the CD4 count (and viral load, if available) data. The development of an episode of PTB after six months of ART, without other clinical and immunological evidence of disease progression, should NOT be regarded as representing ART failure. Extrapulmonary TB should be considered as indicative of ART failure, although simple lymph node TB or uncomplicated pleural disease may be less significant than disseminated TB. If the response to TB therapy is good, the decision on switching to a second-line regimen can be delayed until ATT has been completed. Close monitoring is needed and adherence support should be reinforced.

7.6 Second-line ART in Patients with TB

There are significant drug interactions between PIs and rifampicin. This means that there are limited options for patients who develop TB while on PIs, or in whom TB indicates failure of the first-line regimen and who require PI-based therapy. Unboosted PI cannot be used with rifampicin-containing TB regimens because PI levels are subtherapeutic. If a patient needs to be switched to or is already on a PI-based regimen, 400 mg lopinavir/400mg ritonavir twice daily in combination can be considered, under close clinical and laboratory supervision for hepatotoxicity. Recommendations and precautions for the use of PI-based regimens in combination with rifampicin in women of child-bearing potential and pregnant women are the same as for other TB patients.

7.7 TB-HIV coordination is an integral component of HIV management. The coordination linkages encompass referral of TB suspects from counselling and testing centres to RNTCP, referral from RNTCP to ICTC for HIV testing, and referral and cross-referral of patients to/from ART centres to/from RNTCP for ATT and for HIV care and treatment.

See Annex- 5: Common drug interactions with ARVs

A8 Section

What to Expect in the First Six Months of Therapy

The first six months of ART are critical. Although clinical and immunological improvement is expected, it is not always apparent and the drugs may have side-effects. Some patients may not respond as expected or may even deteriorate clinically at first. Complications are the most common in the first few weeks after the initiation of ART in patients with severe immunodeficiency. It takes time for HIV viral replication to be controlled by ART and for the immune system to be strengthened. It also takes time for the reversal of the catabolism associated with HIV infection, particularly in patients with HIV-associated wasting. As a patient with advanced disease recovers immune function, there may be exacerbation of previously sub-clinical co-existing infection (e.g. TB), resulting in an apparent worsening of the disease. This is NOT due to failure of the therapy, but to the success of ART and the resulting immune reconstitution. It is important to allow for sufficient time on therapy before judging the effectiveness of ART and considering the possibility of IRIS in patients with worsening disease in the first few months of ART.

8.1 **CD4 recovery:** In most patients, the CD4 cell count rises with the initiation of ART and immune recovery. However, this may be blunted if the baseline CD4 count is low. In general, the lower the baseline CD4 count is at the start of ART, the longer it will take for the count to increase with time. In some patients, the count may never exceed 200 cells/mm^3 even with clinical improvement. In those who have achieved a substantial peak response, a subsequent progressive decline in the CD4 count in the absence of intercurrent illness indicates an immunological failure (determined by the trend of regular six-monthly CD4 counts).

8.2 **Early ARV toxicity:** First-line drug toxicities fall into two categories. Early toxicity usually presents in the first few weeks to months of ART. Early and potentially severe toxicities such as hypersensitivity to NNRTIs (EFV and NVP) normally occurs within the first few weeks of therapy and AZT-related anaemia and neutropenia typically presents in the first few months of therapy (*See section 9.0)*.

8.3 **Mortality on ART:** While ART significantly decreases mortality; the risk of death is higher in the first six months than during the subsequent period on therapy, particularly when patients start ART with clinical stage 4 events, severe immunosuppression and very low CD4 counts.

8.4 **Immune reconstitution inflammatory syndrome:** This is a spectrum of clinical signs and symptoms resulting from the body's ability to mount an inflammatory response associated with immune recovery. Antiretroviral therapy partially restores immune defects caused by chronic HIV infection, including the restoration of protective pathogen-specific immune responses. The protective response sometimes causes (atypical) inflammatory manifestations to concurrent infective or non-infective conditions, e.g. TB, MAC or CMV. Clinically, IRIS manifests itself as the occurrence or worsening of clinical and/or laboratory parameters, despite a favourable CD4 count (and viral load). The temporal association between the commencement of HAART (or change from a previously failing regimen) and the development of an unusual clinical phenomenon often provides a strong clue to the diagnosis of IRIS.

Experience has shown IRIS can manifest itself in a variety of ways. **In India, the agreed practical definition of IRIS would be the "occurrence or manifestations of new OIs or existing OIs within six weeks to six months after initiating ART; with an increase in CD4 count".**

8.4.1 The following points help in the diagnosis of IRIS:

- Temporal association between the initiation of ART and the development of clinical phenomena (mostly within 3 months).
  - Typically, IRIS occurs within 2–12 weeks of the initiation of ART, although it may present later (usually between 6 weeks to 6 months)
  - The incidence of IRIS is estimated to be 10% among all patients in whom ART has been initiated; and up to 25% among those who have started ART and who have a CD4 cell count of below 50 cells/mm^3
- Unusual clinical manifestations in patients responding to ART include:
  - Unexpected localized disease, e.g. lymph nodes (appearance or enlargement and/or suppuration), or involving liver or spleen
  - Exaggerated inflammatory reaction, e.g. severe fever, with exclusion of other causes
  - Painful lesions
  - Atypical inflammatory response in affected tissues, e.g. granulomas, suppuration, necrosis
  - Perivascular lymphocytic inflammatory cell infiltrate
  - Progression of organ dysfunction or enlargement of pre¬-existing lesions
  - Development or enlargement of cerebral space-occupying lesions after treatment for cerebral cryptococcosis or toxoplasmosis
  - Progressive pneumonitis or the development of organizing pneumonia after treatment for pulmonary MTB or PCP
  - Onset or worsening of uveitis/vitritis after the resolution of CMV retinitis
  - Fever and cytopenia after treatment for disseminated MAC

8.4.2 The identified risk factors for infectious IRIS are

- An active or sub-clinical infection by opportunistic pathogens
- The antigens of non-viable microorganisms (e.g. Cryptococus and CMV) are all possible targets for an immunopathological response
- A CD4 count of below 50/mm^3 prior to the initiation of HAART
- Being ART naïve
- Starting ART in close proximity to the diagnosis and initiation of treatment for an OI (should first treat and stabilize the OI, then start ART)

Non-infectious IRIS includes Guillain-Barre Syndrome, autoimmune thyroiditis and sarcoidosis. The differential diagnosis for IRIS includes active OI, ARV drug failure, ARV drug toxicity or failure of anti-microbial therapy if the patient is already on the treatment. Culturing the microorganism in body fluids may provide clues to an active OI, which would warrant antimicrobial therapy.

8.4.3 Treatment of IRIS

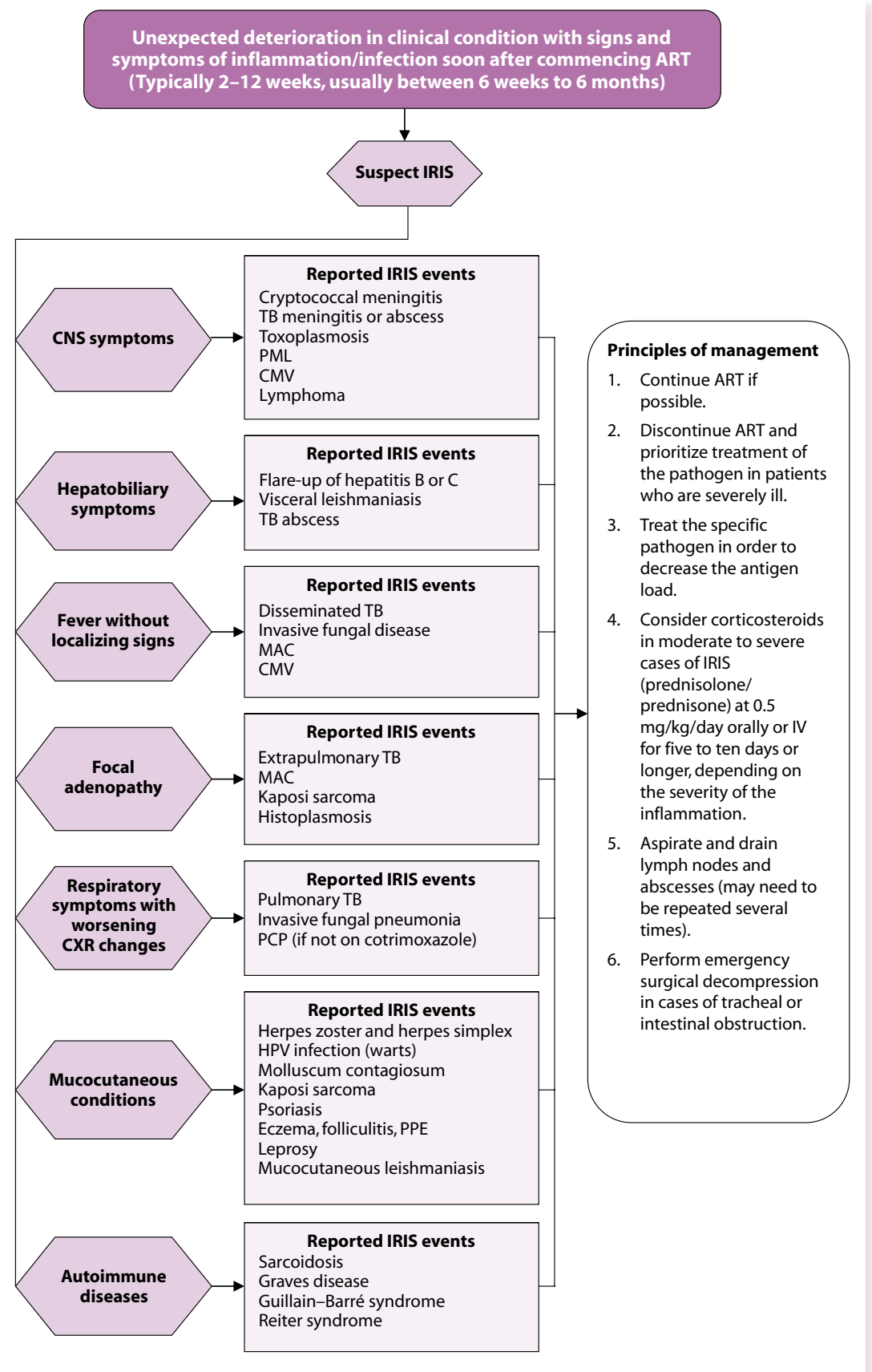
Treatment of IRIS should be referred to a tertiary setting/experienced HIV physician for management.

There are no standard guidelines for the treatment of IRIS. There is very limited information on the effectiveness of various interventions for managing it and little evidence from randomized clinical trials. Most cases resolve without any additional treatment. Milder forms of IRIS resolve with continuing anti-infective therapy and HAART. In the majority of cases, HAART can be safely continued and need not be interrupted. In general, most clinicians prefer to continue ART if the CD4 count is below 100/mm3 or if the patient presents with IRIS months after the initiation of HAART.However, the discontinuation of ART should be considered if the inflammatory responses are considered life-threatening (e.g. intracranial IRIS leading to encephalitis, cerebritis, perilesional cerebral oedema and pulmonary IRIS with ARDS/acute respiratory distress syndrome), or are unresponsive to steroids. Discontinuation of the treatment should also be considered if the pathogens involved are not amenable to specific antimicrobials (e.g. Parvovirus B19, polyomavirus JC casuing PML/progressive multifocal leukoencephalopathy), or if ART toxicity is the main differential diagnosis (e.g. hepatitis).

Non-steroidal anti-inflammatory drugs (NSAIDs) are helpful in controlling inflammation and fever associated with IRIS. However, in severe IRIS, a short course of oral prednisolone is required to alleviate the symptoms. The

dosage and duration of treatment required is variable and should be judged clinically. Severe disease requires at least 1–2 mg of prednisolone per kg body weight. Thalidomide has also been tried effectively in some patients.

Suspect and diagnose IRIS



Note: Refer to NACO OI Guidelines, May 2007. (Chapter 10, p 71 for management of IRIS)

A9 Section

Antiretroviral Drug Toxicity

9.1 ARV drugs are associated with a broad range of toxicity, ranging from low-grade intolerance, which may be self-limiting, to life-threatening side-effects. Differentiating between complications of HIV disease and ART toxicity is sometimes difficult. Alternative explanations should be considered before it is concluded that the symptoms are related to ART toxicity. The factors to be considered include intercurrent illness (e.g. hepatitis A and malaria) and reactions to medications other than ARV drugs (e.g. Isoniazid-induced hepatitis or cotrimoxazole-induced rash). Most of the toxicity/side-effects can be adequately co-managed with efficient clinical monitoring at all levels of the health care system.

9.2 As a general principle, mild toxicities do not require the discontinuation of ART or drug substitution. Symptomatic treatment may be given. Moderate or severe toxicities may require substitution of the drug with another of the same ARV class, but with a different toxicity profile. Severe life-threatening toxicity requires discontinuation of all ARV drugs until the patient is stabilized and the toxicity is resolved.

9.3 Regardless of severity, toxicities may affect adherence to therapy. A proactive approach is required to manage toxicity.

- Discuss potential side-effects of the ART regimen with the patient before initiation and during the early stages of treatment.
- Offer support during minor and major adverse events.
- Ensure that the patient is familiar with the signs and symptoms of toxicities that are serious and require immediate contact with the clinical team, especially in the case of NVP-associated Stevens–Johnson syndrome, hepatitis, lactic acidosis or ABC-associated hypersensitivity reaction.

The side-effects of ARVs need to be differentiated from manifestations of a new OI and IRIS. The management of ART toxicities is based on clinical and laboratory monitoring.

9.4 What Toxicities to Expect after Commencing First-line ART

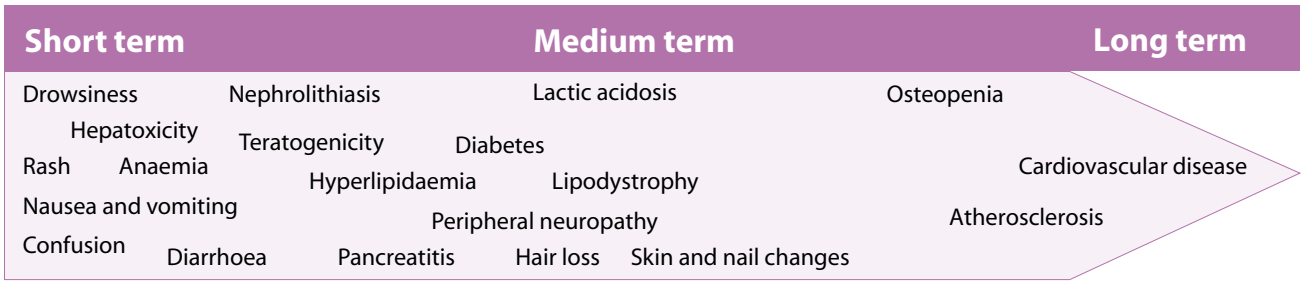


Table 22: Side-effects and common causes

Time	Side-effects and toxicities	Common causes
Short term (the first few weeks)	Gastrointestinal toxicities, including nausea, vomiting and diarrhoea	AZT, TDF, PIs
	Rash (Most rashes occur within the first 2–3 weeks.)	NVP EFV Abacavir PIs (rarely)
	Hepatotoxicity (More common in hepatitis B or C co-infection)	NVP, EFV PIs
	Drowsiness, dizziness, confusion and vivid dreams (Normally self-resolving but can take weeks to months)	EFV
Medium term (the first few months)	Anaemia and neutropenia Sudden and acute bone marrow suppression can occur within the first weeks of therapy or present as a slow onset of progressive anaemia over months	AZT
	Hyperpigmentation of skin, nails and mucous membranes	AZT
	Lactic acidosis (More common after the first few months, most commonly associated with d4T)	d4T, ddI, AZT
	Peripheral neuropathy (More common after the first few months)	d4T, ddI
	Pancreatitis (Can occur at any time)	ddI
Long term (after 6–18 months)	Lipodystrophy and lipoatrophy	d4T, ddI, AZT PIs
	Dyslipidaemia	d4T, EFV, PIs
	Diabetes	IDV
	Skin hair and nail abnormalities	PIs, especially IDV

(See Annex 4: Clinical signs and symptoms and management of adverse effects of antiretroviral drugs)

9.5 Substituting within a First-line Antiretroviral Drug Regimen due to Drug Toxicity

A drug may need to be substituted to simplify the regimen so as to improve adherence, manage side-effects/ toxicities and/or reduce the cost of the regimen. The commonest example of substitution for avoiding long-term toxicity is substituting from d4T and AZT to ABC or TDF.

Table 23: Major toxicities caused by first-line ARV regimens and recommended drug substitutions

Regimen	Toxicity	Drug substitution
D4T/3TC/NVP	• d4T-related neuropathy or pancreatitis • d4T-related lipoatrophy • NVP-related severe hepatotoxicity • NVP-related severe rash (but not life-threatening) • NVP-related life-threatening rash (Stevens Johnson syndrome)	• Substitute with AZT • Substitute with TDF or ABC (if available) • Substitute with EFV (except in first trimester of pregnancy) • Substitute with EFV • Substitute with PI or use "triple NRTI approach" which reserves PI for second-line treatment
AZT/3TC/NVP	• AZT-related persistent GI intolerance or severe haematological toxicity • NVP-related severe hepatotoxicity • NVP-related severe rash (but not life-threatening) • NVP-related life-threatening rash (Stevens–Johnson syndrome)	• Substitute with d4T • Substitute with EFV (except in pregnancy. In this situation switch to NFV, LPV/r or ABC.) • Substitute with EFV • Substitute with PI or use "triple NRTI approach" which reserves PI for second-line treatment
D4T/3TC/EFV	• d4T-related neuropathy or pancreatitis • d4T-related lipoatrophy • EFV-related persistent CNS toxicity	• Substitute with AZT • Substitute with TDF or ABC • Substitute with NVP
AZT/3TC/EFV	• AZT-related persistent GI intolerance or severe haematological toxicity • EFV- related persistent CNS toxicity	• Substitute with d4T • Substitute with NVP

Notes :

- The general principle is that single-drug substitution for toxicity should be made within the same ARV class. [e.g. substitution of d4T with AZT or TDF (for neuropathy), AZT with d4T or TDF (for anaemia), or EFV with NVP (for CNS toxicity or in pregnancy)].
- Substituting d4T may not reverse lipodystrophy but may slow its progression. Besides AZT and TDF, ABC or ddI are acceptable alternatives but are not available in the national programme.
- If a life-threatening toxicity occurs, all ART should be stopped until the toxicity has resolved and a revised regimen commenced when the patient has recovered.

A10 Section

ARV Treatment Failure and when to Switch

10.1 The clinical goals of HIV treatment are optimally accomplished through consistent high-level adherence to HAART and sustained suppression of the viral load. However, as a result of the need for lifelong therapy and HIV's prodigious replication rate and error-prone reverse transcriptase, varying amounts of drug resistance are common in individuals undergoing treatment. It is now well known that even with good adherence levels, resistance occurs. HIV drug resistance evolves naturally due to the selective pressure from drugs or from the immune system.

10.2 Drug resistance occurs when HIV replication is not fully suppressed. This is frequently linked to non-adherence to ARV therapy.

- Resistant viruses can spread and affect ARV therapy. The transmission of ARV-resistant strains is of increasing concern in countries where ARV is widely used.
- Resistance can be contained. Its occurrence can be reduced or prevented by an appropriate and careful choice of treatment, intense support to ensure adherence, monitoring for resistance and reinforcing positive prevention with condom use.

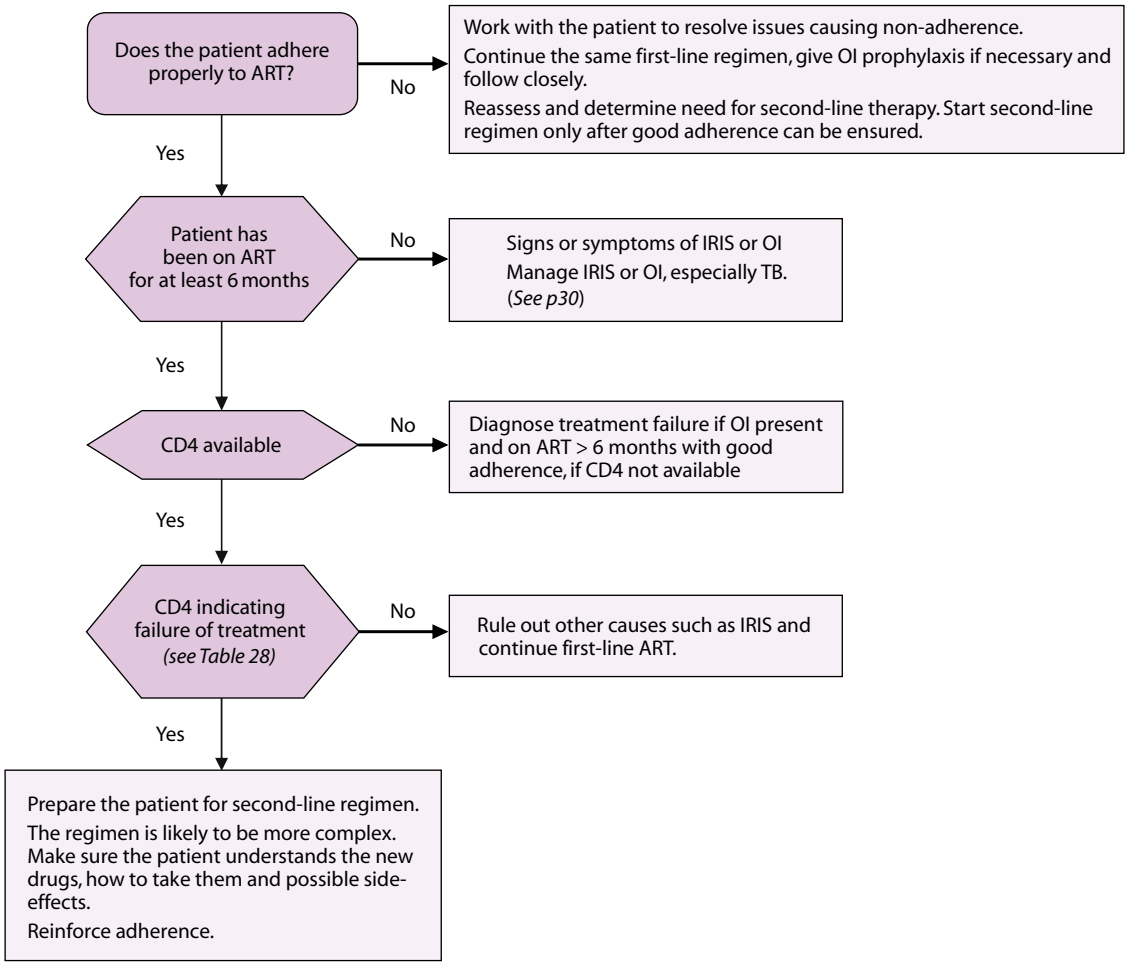
10.3 Failure to access care and discontinuation of or non-adherence to ART are the most important factors associated with the progression of HIV disease. Nationally, there is a need to define drug resistance qualitatively and quantitatively through surveillance and monitoring conducted in accordance with international standards. Such studies have already been initiated by NACO and WHO. The outcome of these studies will be used to guide programmatic and treatment options.

Prevention of the emergence of HIV drug resistance (HIV DR) is accorded a high priority and is a crucial component of the National ART Programme

10.4 Identifying Treatment Failure

The decision on when to switch from first-line to second-line therapy is critical. If the decision is made too early, the months or years of any potential survival benefit from an effective first-line therapy may be lost. If the decision is made too late, the effectiveness of second-line therapy may be compromised and the patient may be put at an additional risk of death. The time of switching drugs is dictated by the failure of treatment, which can be measured in three ways: clinically, immunologically and virologically. However, the definitions of these criteria represent different biological endpoints. It is not clear which criterion is optimal, individually or together with others. There is a need for consensus and standardization on the different ways of identifying failure. (WHO, 2006). In ALL cases, adherence counselling and clinical judgement must form a part of the decision-making.

10.4.1 Determining ART failure



Notes:

- Switching to second-line regimen is not an emergency. Review the patient's OI prophylaxis management. Patients on a failing regimen with WHO stage 2, 3, 4 disease or with a CD4 count < 200 cells/mm^3 need to restart cotrimoxazole.
- While a failing regimen may retain some anti-HIV activity; the longer the patient remains on a failing regimen, the more resistance mutations accumulate, reducing the chances of success of the second-line regimen. The decision to switch drugs is based on clinical, immunological or virological definitions of failure (presented below) and the availability of second-line ARV drugs.

10.4.2 As mentioned earlier, antiretroviral treatment failure can be defined virologically, immunologically or clinically, and in most instances, one type of failure follows the other. There is a delay between virological and immunological failure, which increases the risk of exposing the HIV virus to a failing regime, leading to the development of further cross-resistance and compromising the efficacy of the second-line regimen.

10.4.3 The progression of clinical disease should be differentiated from IRIS, which is characterized by the appearance of signs and symptoms of an OI a few weeks after the initiation of HAART in the setting of advanced immunodeficiency. These symptoms are an inflammatory response to previously sub-clinical OI. It is also possible to have atypical presentations of some OIs.

10.4.4 The failure of treatment cannot be diagnosed on the basis of clinical criteria in the first six months of ART. Clinical events that occur before the first six months of therapy often represent IRIS and not failure.

10.5 The following definitions of ART failure are used:

Table 25: Clinical, immunological and virological definitions of treatment failure for first-line regimen (WHO, 2006)

Clinical failure[i]	New or recurrent WHO stage 4 condition, after at least 6 months of ART[ii, iii]
Immunological failure[4]	• Fall of CD4 count to pre-therapy baseline (or below) • 50% fall from the on-treatment peak value (if known) • Persistent CD4 levels below 100 cells/mm [iii, v]
Virological failure	Plasma viral load > 10,000 copies/mL[vi]

Notes:

i) Current event must be differentiated from IRIS.

ii) Certain WHO clinical stage 3 conditions (e.g. pulmonary TB, severe bacterial infections) may indicate treatment failure and thus requirsecond-line therapy to be considered.

iii) Some WHO clinical stage 4 conditions (lymph node TB, uncomplicated TB pleural disease, oesophageal candidiasis, recurrent bacterial pneumonia) may not indicate treatment failure and thus second-line therapy need not be considered.

iv) Without any concomitant infection causing transient CD4 cell count decrease.

v) Some experts consider persistent CD4 cell counts of below 50/mm^3 after 12 months of ART to be more appropriate.

vi) The optimal viral load value at which ARV drugs should be switched has not been defined. However, values of more than 10,000 copies/mL have been associated with subsequent clinical progression and an appreciable decline in the CD4 cell count.

10.5.1 **Clinical failure**: There should be a reasonable trial of first-line therapy, lasting at least 6–12 months, before concluding that the ARV regimen is failing on the basis of clinical criteria. Adherence should be assessed and optimized, intercurrent OI treated and resolved, and IRIS excluded before drawing such a conclusion.

The development of a new or recurrent WHO stage 3 or 4 condition while on treatment (after the first six months) is considered functional evidence of the progression of HIV disease. This is referred to as T staging, where T refers to the staging event on treatment. The assumption is that with immune restoration on ART and the subsequent progressive immunodeficiency with a failing ART regimen, the clinical events signaling immune failure will be the same as those marking advanced and then severe immunodeficiency without ART eg. WHO Clinical stage 3 and 4. Table 26 indicates how clinical staging on ART can be used as an indicator of failure and may facilitate the decision on whether to switch therapy.

Table 26: Clinical and CD4 cell count definitions of treatment failure in adults and adolescents

Clinical signs of treatment failure	CD4 cell criteria for treatment failure
• Occurrence of new OIs or malignancy signifying clinical disease progression. This must be differentiated from IRIS, which can occur in the first 3 months of ART[i] • IRIS does not signify treatment failure and the OI should be treated as usual, without changes in the ART regimen • Recurrence of previous OI[ii] • Onset or recurrence or WHO stage 3 conditions (including but not restricted to HIV wasting, chronic diarrhoea of unknown aetiology, prolonged fever of unknown aetiology, recurrent invasive bacterial infections, or recurrent/persistent mucosal candidiasis)	• Return of CD4 count to pre-therapy baseline or below, without other concomitant infection to explain transient CD4 count decrease[iii] • >50% (2006 WHO guidelines) fall from on-treatment CD4 peak level without other concomitant infection to explain transient CD4 count decrease[iii]

Notes:

i IRIS is characterized by the appearance of signs and symptoms of OIs a few weeks after the start of HARRT in the setting of advanced immunodeficiency, as an inflammatory response to previously subclinical OI. This immunological reconstitution may also lead to the development of atypical presentations of some OIs.

ii The recurrence of TB may not represent HIV disease progression as re-infection can occur. Clinical evaluation is necessary.

iii If the patient is asymptomatic and treatment failure is being defined by the CD4 count alone, consider taking a confirmatory CD4 count, if resources permit.

Table 27: Clinical staging events to guide decision-making on switching

New or recurrent event on ART[a]	Recommendations	Additional Management Options
Asymptomatic (T1)	Do not switch regimen	• Maintain schedule follow-up visits, including CD4 monitoring (if available) • Continue to offer adherence support
Stage 2 event (T2)	Do not switch regimen[b]	• Treat and dmanage staging event • Assess and offer adherence support • Check if on treatment for at least six months • Assess continuation of reintroduction of OI prophylaxis • Schedule earlier visit for clinical review and consider CD–4 (if available)[c]
Stage 3 event (T3)	Consider switching regimen[bd]	• Treat and manage staging event and monitor response • Assess and offer adherence support • Check if on treatment for at least six months • Check CD4 cell count (if available)[cd] • Assess continuation of reintroduction of OI prophylaxis
Stage 4 event (T4)	Switch regimen[be]	• Treat and manage staging even and monitor response • Check if on treatment for at least six months • Assess continuation or reintroduction of OI prophylaxis • Check CD4 cell count (if available)[c] • Assess and other adherance support

a Refers to clinical stages while on ART for at least six months (termed T1, T2, T3, T4)

b Differentiation of opportunistic infections from immune reconstitution inflammatory syndrome is necessary.

c Treat and manage the staging event before measuring CD4 cell count.

d Certain WHO clinical stage 3 conditions (e.g. pulmonary TB, severe bacterial infections) may be indicators of tratment failure and thus require consideration of second-line therapy; response to appropriate therapy should be used to evaluate the need for switching of therapy.

e Some WHO clinical stage 4 conditions (lymph node TB, uncomplicated TB pleural disease, oesophageal candidiasis, recurrent bacterial pneumonia) may not be indicators of treatment failure and thus do not require consideration of second-line therapy, response to appropriate antimicrobial therapy should be used to evaluate the need to switch therapy.

TB can occur at any CD4 level and does not necessarily indicate ART failure. The response to TB therapy should be used to evaluate the need to switch ARV drugs. In the case of pulmonary TB and some types of extrapulmonary TB (e.g. simple lymph node TB or uncomplicated pleural disease), the response to TB therapy is often good and the decision to switch ARV drugs can be postponed and monitoring can be stepped up. This also applies if severe and/or recurrent bacterial infections (as stage 3 or 4 events) or oesophageal candidiasis respond well to therapy.

10.5.2 Immunological failure: The working definitions of immunological failure are:

- A return to, or fall below, the pre-therapy CD4 baseline after at least 6 months of therapy
- A 50% decline from the on-treatment peak CD4 value (if known)
- A persistent CD4 count of less than 100 cells/mm^3 after 6–12 months of therapy

The CD4 cell count is the strongest predictor of HIV-related complications, even after the initiation of therapy. The baseline pre-treatment value is informative: lower CD4 counts are associated with smaller and slower improvements in the count over time. CD4 cell counts can also be used to determine when not to change therapy. For example, in a patient with a new clinical stage 3 event, switching is not be recommended if the CD4 cell count is greater than 200 cells/mm^3.

10.5.3 **Virological failure**: This is an incomplete suppression of the virus and is defined as a PVL value of more than 10,000 copies/mL (WHO 2006 guidelines) at six months after the initiation of ART. Viral rebound after being undetectable is also considered as virological failure. A low-level viral rebound (<500–1000 copies/mL), termed *blips*, usually indicates a statistical variation in the determination of PVL and not the need to alter therapy. The viral load remains the most sensitive indicator of ART failure. Recognizing early failure facilitates the decision to switch drugs before multiple resistance mutations develop to drugs of the first-line regimen.

In general, the clinical status, CD4 cell count and PVL (if available) can be used in an integrated fashion to determine whether HIV disease is progressing while a patient is on ART; and whether a change should be made from first-line to second-line therapy. Although the national programme does not have provision for second-line drugs at present, guidance is essential, considering that patients may seek advice from the private sector or buy drugs out-of-pocket. Table 27 provides guidance on deciding when to change the treatment regimen on the basis of clinical status in relation to the CD4 count alone or to the CD4 count plus viral load data. Clinical judgment is an important part of the decision-making process.

Table 28: Integrating clinical status, CD4 counts and viral load to guide switching

Treatment failure criteria	WHO stage 1	WHO stage 2	WHO stage 3	WHO stage 4
CD4 failure[i] (viral load testing not available)	Do not switch regimen. Follow patient for development of clinical signs or symptoms. Repeat CD4 count in 3 months.	Do not switch regimen. Follow patient for evidence of further clinical progression. Repeat CD4 in 3 months.	Consider switching[ii] to second-line regimen.	Recommend switching[ii] to second-line regimen.
CD4 failure and virological failure[iii]	Consider switching to second-line regimen.	Consider switching to second-line regimen.	Recommend switching to second-line regimen.	Recommend switching to second-line regimen.

Notes:

i CD4 failure is defined as a fall to below the pre-treatment baseline value or a 50% drop from the on-treatment peak level or persistent levels below 100 cells/mm^3.

ii Switching from first-line to second-line regimen is not recommended until the first-line regimen has been given sufficient time to succeed. This should be a minimum of six months. Since only one second-line regimen is available in most circumstances, premature switching should be avoided.

iii Virological failure is provisionally defined as a plasma HIV-1 RNA level > 10,000 copies/mL after a minimum of six months of therapy.

10.6 Managing Failure

Identifying the cause of failure is important before deciding to modify the ART regimen. The following points need to be assessed.

I. Adherence: A detailed assessment of adherence needs to be made. The reasons for non-adherence need to be explored. Unless these reasons are identified, a patient will also find it difficult to adhere to the second-line regimen.

II. Drug-drug interactions: Assessing whether the patient is concomitantly taking medications which interfere with ARV activity is important. For example, many patients may not reveal that they take herbal treatments along with the prescribed ART regimen.

III. Continuing high-risk behaviour: If a patient continues to engage in high-risk behaviour, super-infection with a drug resistant virus may lead to treatment failure.

Once resistance is confirmed, an experienced referral HIV physician could design a second-line ART regimen, if it is accessible, affordable and available. However, with the current operational limitations of the national treatment programme, a patient suspected to have treatment failure should be managed as best as possible by the ART centre staff and linked NGOs/positive network. The effort should be to ensure non-transmission of the resistant virus (through positive prevention and safer sex), provide psychosocial support and counselling, offer palliative and home care when necessary, and provide prophylaxis and treatment of OI.

A11 Section

Choice of ARV Regimens in the Event of Failure of First-line Regimens

11.1 During the development of the NACO technical guidelines, it was acknowledged that the private sector too provides for ARV therapy. Although second-line regimens are currently not available under the national programme, experience has shown that the private sector concurrently uses second-line ARV drugs, such as ABC and PIs, and this has resulted in a cohort of non-naïve treatment experience patients. It is, therefore, important to provide guidance on the choices of second-line regimens in the event of the failure of first-line regimens. **A second-line regimen should be recommended only by an experienced HIV physician**, after he/she has determined that it is a case of true treatment failure.

11.2 When failure has been identified clinically or immunologically, many patients can be expected to have significant NRTI resistance at the time of switching. Thus, in the decision-making for a second-line regimen with maximal antiviral activity, one has to consider nucleoside class cross-resistance and drug interactions (*see table 29*). Several points to note are:

- Cross resistance exists between d4T and AZT; thus NRTI-component in the second-line regimens should be either ddI/ABC or TDF/ABC.
- High level AZT/3TC resistance reduces susceptibility to ABC.
- TDF can be compromised by multiple nucleoside analogue mutations (NAMs) but often retain activity against nucleoside-resistant viral strains.
- ddI/ABC and TDF/ABC may facilitate evolution of the K65R drug resistance mutation, which mediates resistance to non-AZT NRTIs.
- NNRTI (such as EFV and NVP): usually there is complete cross-resistance.

Table 29: Expected resistance mutations with different NRTI backbone

Failing NRTI backbone	Mutations
AZT or d4T + 3TC and AZT + 3TC + ABC	M184V And then successive NAMs (cumulative, the longer one waits to switch)
TDF + 3TC	K65R and/or M184V
ABC + 3TC	L74V > K65R and/or M184V
AZT or d4T + ddI	TAMs, Q151M, T69ins
TDF + ABC and TDF + ddI	K65R

11.3 Ideally, second-line regimens should include at least three active drugs; one of them from a new class, in order to increase the likelihood of the success of the treatment and to minimize the risk of cross-resistance. The PI class should be reserved for second-line treatments.

11.4 Decide What to Give for Second-line Regimen

Second-line regimens should be prescribed by experienced HIV physicians or in consultation with them. The following flow chart provides guidance.

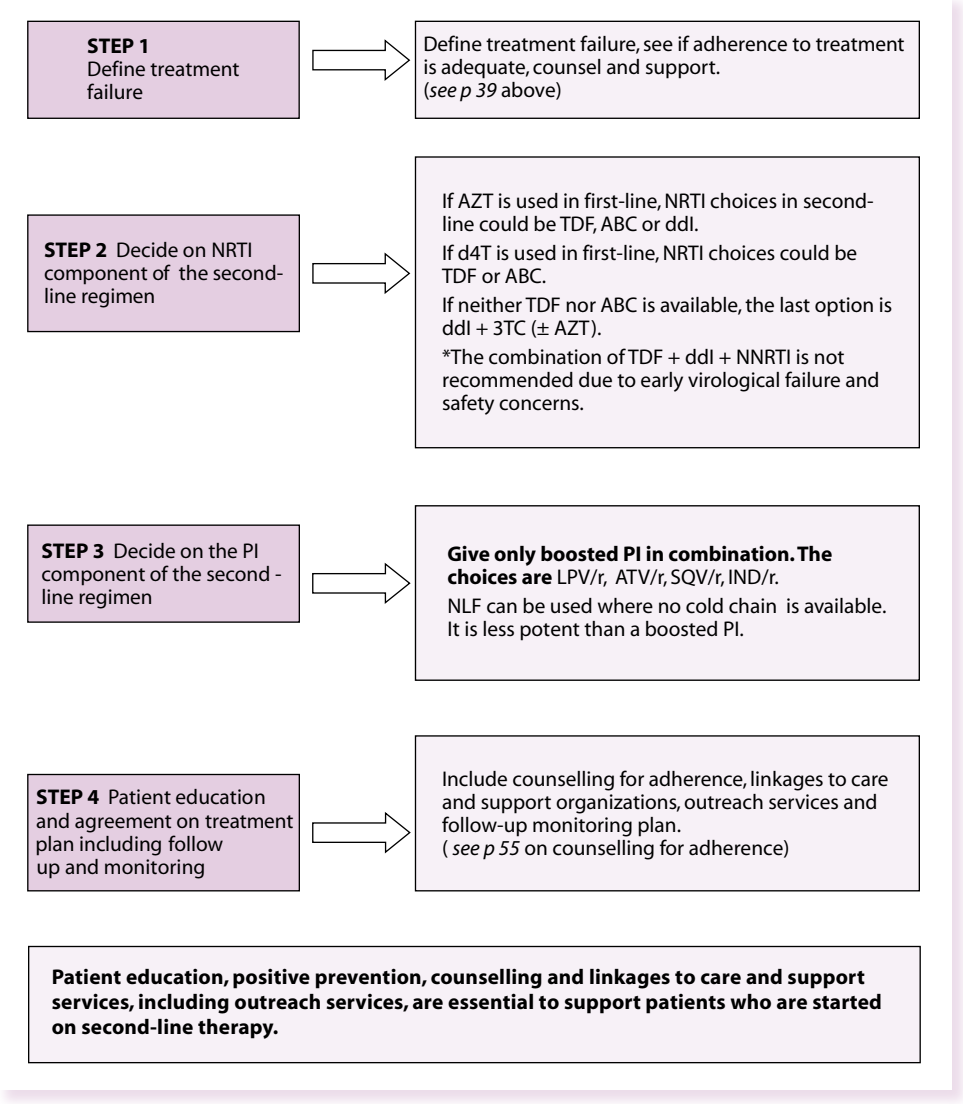


Table 30: List of regimens and alternatives

First-line regimen		Second-line regimen	
		NRTI component	PI component[i]
Standard Regimens	AZT + 3TC + NVP	**Choices:** 1st TDF + ABC or 2nd ddI + ABC or 3rd TDF + AZT (± 3TC)[ii]	Choices: 1st LPV/r (heat-stable) 2nd ATV/r 3rd SQV/r 4th IND/r 5th NLF where no cold chain available
	AZT + 3TC + EFV		
	D4T + 3TC + NVP		
	D4T + 3TC + NVP		
Special circumstances	TDF + 3TC + NVP	**Choices:** 1st ddI/ABC 2nd ddI/AZT (± 3TC)[ii]	
	TDF + 3TC + EFV		

Notes:

i A ritonavir-boosted PI is the core of the second-line regimen. NLF can be used but is considered less potent than an RTV-boosted PI.

ii 3TC can be considered to be maintained in the second-line regimen to potentially reduce viral fitness, confer residual antiviral activity and maintain pressure on the M184V mutation to improve viral sensitivity to AZT or TDF. AZT may prevent or delay the emergence of the K65R mutation. The disadvantage is the very high pill burden, which may create practical difficulties.

A12 Section

Considerations for ART in IDUs or PLHA under Substitution Programmes

12.1 Principles of Comprehensive Care for IDUs

The key components of comprehensive care for IDUs are:

- Assessment and management of physical and psychological co-morbidities, including viral hepatitis and psychiatric conditions (such as depression).
- Assessment of the patient's treatment priorities, goals and readiness to start ART if it is medically indicated.
- Opioid substitution therapy (OST).

Since the clinical and CD4 criteria for initiating ART in substance-dependent patients are no different from other PLHAs, IDUs (current or previous) who are eligible for ART should receive care and treatment as per the national protocol.

12.2 Linkage between Harm-reduction Programmes and ART Centres

As HIV-infected IDUs have special needs with regard to drug use, ART should be given as part of a comprehensive package of prevention (including harm reduction), care and support, and treatment. Harm-reduction programmes have trained staff (social workers, counsellors and outreach workers), who are experienced in reaching out to and communicating with IDUs, and have established credibility and trust. The linkage between ART centres and harm reduction programmes should be established for the following:

- Outreach to potential clients for HIV testing and prevention of transmission of HIV.
- Support for ART adherence.
- Follow-up of patients who drop out of care or default on scheduled visits.
- Implementation of OST for suitable patients.
- Patient education and peer support.

12.3 ART for HIV-infected IDUs

Substance-using PLHA (current or previous) who are medically eligible for ART should be given care and treatment as per the national guidelines. Refer to the harm reduction programme if required.

Table 31: Initiating ART in substance-using patients	
Initiating ART	The criteria for initiating ART in substance-using patients are the same as in the case of other patients with HIV • Before starting ART, specific factors that may affect the timing of initiation and the choice of ART should be considered: social instability, active use of illicit drugs and the presence of co-morbidities, such as mental problems and co-infection with hepatitis viruses • Unavailability of OST or active use of illicit drugs should not hinder access to ART for those in need of treatment • Effective links between ART and harm-reduction programmes are essential. • Initiate ART once the patient has been adequately prepared and counseled for treatment adherence • Spending adequate time on preparing patients for ART, and helping them understand the treatment goals, need for adherence and lifelong nature of ART will maximize treatment outcomes
Choice of ART	National regimens can be chosen for the majority of IDUs. The choice of specific ARV drugs depends on: • Co-morbidities (especially hepatitis B/C and psychiatric disorders). • Drug interactions (methadone) • Adherence.
Preferred first-line regimen	**AZT + 3TC + EFV** if liver dysfunction is noted **AZT + 3TC + NVP** if patient is stable; monitor closely for hepatitis With this combination, 3TC is the only drug with anti-HBV activity (thus, there is a higher risk of HBV resistance to 3TC)
Choice of NNRTI	Hepatitis C and B infections are extremely common in IDUs. Monitoring hepatotoxicity is strongly recommended in IDUs receiving NNRTI-based ART, especially NVP **Efavirenz** EFV is preferred in patients with clinical and/or laboratory evidence of significant (grade 3 or 4) hepatic dysfunction. It should be used with caution in patients with depression or other significant psychiatric conditions **Nevirapine** NVP is recommended in patients with no other significant co-morbidities, specifically, those with no clinical signs of hepatic dysfunction or increase in hepatic transaminases (grade 3 or 4). Use NVP under close clinical and laboratory (liver enzymes) monitoring
Alternative first-line regimen	**d4T + 3TC + (EFV or NVP)** AZT may be replaced by d4T in any regimen in case of toxicity or other contraindications eg. anaemia **TDF + 3TC + (EFV or NVP)** in special circumstances, for example, if the patient is intolerant to d4T or AZT
Second-line regimen	The recommendations are the same as those for other patients with HIV (*see p 45*)
Adherence	Given a good patient–clinical team relationship and adequate support, IDUs can adhere to ART and have clinical outcomes comparable with those of HIV patients who do not use drugs[13,14]
Buprenorphine	There is no significant drug interaction between the first-line ARV drugs and buprenorphine
Methadone	Methadone is not available as OST in India. WHO has included methadone as part of the Essential Drug List. *See Annex 6* for details on ART and methadone

12.4 Viral Hepatitis and Chronic Liver Disease

Co-infection with HCV is common among HIV-infected IDUs. Chronic, active hepatitis B and alcoholic liver disease are also common. **Hepatotoxicity associated with these conditions complicates the choice of ART.** The NRTIs associated with the greatest hepatotoxicity are AZT, ddI and d4T. Both the NNRTIs available under the national programme can cause hepatotoxicity. Of these, NVP is more commonly associated with severe hepatotoxicity and should be avoided if possible in all patients with chronic liver disease and liver dysfunction. EFV can be administered in full doses in patients with liver insufficiency. PIs are also associated with hepatotoxicity, and the dosing is complex in patients with hepatic insufficiency.

Drugs for treating hepatitis C, such as pegylated interferon (IFN) and ribavirin (RBV), are not currently provided by the national programme. Newer drugs are being developed globally. Patients should be stabilized on ART at a CD4 count of above 200 cells/mm^3 before pegylated IFN and RBV are started. RBV increases AZT levels, and patients should be closely monitored for hepatic toxicity, neutropenia and anaemia.

Causes of hepatic dysfunction other than viral hepatitis need to be considered. Alcohol use/dependency has the same implication for treatment options and monitoring as does viral hepatitis. Where possible, the least hepatotoxic ARV should be used and hepatic enzymes monitored in all patients with hepatic dysfunction.

See section A13, p 51

12.5 Opioid Substitution Therapy

OST is the most effective treatment for opioid dependence, and results in substantially higher retention rates, suppression of drug use and improved psychosocial functioning. Its use in the context of HIV treatment has been associated with improved adherence to and outcomes of treatment. Detoxification and abstinence-based programmes are unlikely to achieve similar levels of clinical effectiveness and may prove counterproductive in the context of ART. If possible, stabilization of substance use with substitution treatment is recommended prior to the commencement of ART.

The outcomes of OST in a structured programme include:

- Decreased heroin use and reduced chaotic drug-taking
- Decreased needle-sharing
- Stabilization of clients' lives
- Improved quality of life and the chance to lead a productive life in the community
- Improved ability to commence and adhere to ART

OST programmes in India use buprenorphine sublingual tablets. Methadone and buprenorphine are both included in the WHO Essential Drugs List.

12.5.1 Buprenorphine

Buprenorphine is administered as a single daily dose in the range of 8–34 mg/day. The average dose for most patients is 16 mg/day, but doses up to 34 mg/day may be required. Tablets should be placed under the tongue until they dissolve. Swallowing the tablets reduces the bioavailability of the drug. There are two sublingual formulations, buprenorphine alone and buprenorphine combined with naloxone. The addition of the opioid antagonist, naloxone, is intended to discourage injecting of the dissolved tablets.

Interactions between ART and buprenorphine are not as well researched as those involving methadone. Serum levels of buprenorphine are reduced by EFV and some PIs (e.g. IND and SQV), but **no dosage adjustment** of buprenorphine is recommended. However, emerging evidence indicates that certain PIs, including RTV and ATV, inhibit buprenorphine metabolism, resulting in a clinically significant effect. The dose of buprenorphine may need to be reduced in this context.

Table 32: Interactions between buprenorphine and ARVs

ARV	Effect On Bruprenorphine	Effect On ARV	Comments
NRTIs			
No significant interactions reported			
NNRTIs			
EFV	Buprenorphine concentrations decreased but not significantly[15]	None reported	No dose adjustment of EFV required
PIs			
RTV	Inhibition of buprenorphine metabolism, resulting in a clinically significant increase in buprenorphine levels	None reported	Buprenorphine dose may need to be reduced
ATV			

A13 Section

HIV and Hepatitis Co-infection

13.1 Hepatitis B Co-infection

As Hepatitis B is endemic in India, with varying geographical prevalence, HIV-infected persons especially those with a history of blood transfusion and injecting drug use and a history suggestive of hepatitis will be screened for baseline HBV/HCV status under the national programme. Vaccination may be considered for those attending STI clinics and HIV-infected persons who are found to be HbsAg-negative.

HIV modifies the natural history of HBV infection: higher rates of progression to advanced liver disease occur among persons with HIV/HBV co-infection. The presence of HIV infection is associated with greater rates of progression to cirrhosis. The impact of HBV on the natural history of HIV is less known.

Table 33: Principles of ART in hepatitis B co-infection

Choice of ART	ARVs with anti-HBV activity such as 3TC (or FTC) should be included in the first-line ART regimen for HIV-infected patients who are HBsAg-positive (and HBeAg-positive, if known)
Preferred first-line ART	**AZT + 3TC + EFV** if liver dysfunction is noted **AZT + 3TC + NVP** if patient is stable; monitor closely for hepatitis With this combination, 3TC is the only drug with anti-HBV activity (thus, there is a higher risk of HBV resistance to 3TC)
Alternatives	**d4T + 3TC + (EFV or NVP)** AZT may be replaced by d4T in any regimen in case of toxicity or other contraindications eg anaemia **TDF + 3TC + (EFV or NVP)** if patient is intolerant to AZT or d4T Note: Both TDF and 3TC have activity against HBV
Choice of NNRTI	• EFV is the preferred NNRTI option if liver dysfunction is noted • NVP should be used with care and regular monitoring done in patients who have known HIV/HBV co-infection and grade 1, 2 or 3 increase in ALT/AST • NVP is not recommended for patients with grade 4 or greater increase in ALT/AST
Second-line regimen	3TC should be continued as part of the second-line ART following initial ART failure, even if it was used in the first-line regimen
HBV resistance	• Ideally, 3TC should be used either with TDF or not at all, because HBV resistance to 3TC develops quickly • HBV resistance to 3TC develops in 50% of patients after two years and in 90% after four years of treatment if 3TC is the only active anti-HBV drug in the ART regimen
Therapy outcomes	HBV seroconversion (loss of HBeAg and development of HBeAg) occurs in 11–22% of HBeAg-positive HIV-infected patients who are treated with 3TC for one year.
Hepatic flares	• HBV flares on ART start soon after the initiation of ART as a manifestation of IRIS • Discontinuation of 3TC may also result in hepatic flares

Table 33: Principles of ART in hepatitis B co-infection	
FTC	The rate of suppression of HBV and safety profile and resistance pattern with FTC are similar to those with 3TC. FTC is not provided by the national ART programme.

Notes: Hepatic flares typically present as an unexpected increase in ALT/AST levels and symptoms of clinical hepatitis (fatigue, nausea, abdominal pain and jaundice) within 6–12 weeks of commencing ART. The flares may be difficult to distinguish from ART-induced hepatic toxicity. Drugs active against HBV should preferably be continued during a suspected flare. If it is not possible to distinguish a serious hepatitis B flare from grade 4 drug toxicity, ART should be stopped until the patient stabilizes.

Choice of NNRTIs (NVP or EFV) in hepatitis co-infection: Patients who have hepatitis B or C and/or abnormal liver function at the start of therapy with NVP are at a greater risk of symptomatic events (at six weeks or more of NVP) and asymptomatic increases in AST or ALT. The risk of symptomatic hepatic events, regardless of severity, is the greatest in the first 6 weeks of therapy. However, hepatic events may occur at any time during the treatment. In some cases, patients present with non-specific, prodromal signs or symptoms of fatigue, malaise, anorexia, nausea, jaundice, liver tenderness or hepatomegaly, with or without initial abnormal serum transaminase levels. Serious psychiatric events have been reported in patients treated with EFV. These include severe depression (2.4%), suicidal ideation, aggressive behaviour, paranoid reactions and manic reactions.

13.2 Hepatitis C Infection

Co-infection with Hepatitis C increases the risk of hepatotoxicity with ART. However, the majority of patients with HCV are able to tolerate ART. Where there is a previous history of injecting drug use, HCV and HBV screening should be included in the baseline testing.

The progression of liver disease is greater in the setting of HIV–HCV co-infection. However, as with HBV, the effect of HCV on HIV disease progression is uncertain.

Table 34: Principles of ART in HCV co-infection	
HCV therapy	No ARV drugs are directly active against HCV. However, ART has been shown to delay the progression of HCV liver disease in HCV–HIV co-infection The only effective treatment consists of pegylated IFN and RBV, which are generally not available widely
HCV therapy outcomes	Clinical trial outcomes • HCV genotype 1: 15–28% sustained virological response rates • HCV genotypes 2 and 3: 60–70% virological response rates
Side-effects of IFN	Up to 60% of individuals treated with IFN experience psychiatric problems, mostly commonly depression. Monitor mental health closely
Timing of HCV therapy in relation to ART	• Commence anti-HCV therapy before the CD4 count drops to levels where ART is required, i.e. <200 cells/ mm^3 • If ART is required, the patient should be stable on ART with a CD4 count >200 cells/mm^3 before anti-HCV therapy is considered, in order to get better anti-HCV response rates after immune recovery
Preferred first-line ART regimen	• The choice of NRTI is the same as that for patients without HCV • EFV is the preferred NNRTI where liver dysfunction is noted • NVP should be used with care and regular monitoring in patients who have known HIV–HBV/HCV co-infection and grade 1, 2 or 3 increase in ALT/AST • NVP is not recommended for patients with a grade 4 or higher increase in ALT/AST
Drug interactions	• RBV and d4T/ddI: do not co-administer as there is a risk of pancreatitis/lactic acidosis/ liver decompensation • RBV and AZT: monitor closely for anaemia • IFN and EFV: monitor closely for depression
Hepatic flares	Soon after initiation of ART, as part of IRIS

Notes: It is recommended that HBV and HCV disease be co-managed with specialized departments (gastroenterology/hepatology). As prevention is the mainstay of HCV management, treatment should be made available to IDUs as a part of a package of services, including harm reduction and substitution programmes.

A14 Section

Considerations for ART in Adolescents

According to WHO, adolescence is the period between 10–19 years of age. During this period, healthy HIV-infected adolescents pass through well-described stages of physical, psychological and sexual maturation for which appropriate care and treatment are required. Physicians giving care and treatment to such adolescents should consider the following issues:

- Disclosure
- Developmental delays
- Transition difficulties from childhood to adulthood which may influence choice of appropriate ART regimens
- Adherence issues
- Psychosocial support needs
- Physical and sexual issues

Refer to National Guidelines for HIV Care and Treatment in Infants and Children, NACO November 2006, for more details.

A15 Section

Adherence to ART

The most common cause of ART failure is **poor adherence**. Adherence should be assessed and routinely reinforced by everyone in the clinical team (physicians, counsellors, nurses, pharmacists, peer educators, NGO workers, etc) at each of the patient's visits to the clinic. Studies indicate that 90–95% of the doses should be adhered to for optimal suppression. Lesser degrees of adherence are often associated with virological failure. Maintaining the optimum level of adherence is difficult.

Factors associated with poor adherence include a poor patient–clinician relationship, high pill burden, forgetfulness, mental depression, lack of patient education, inability of patients to identify their medications, drug toxicity, cultural factors (e.g. religious fasting), beliefs about treatment and the impression of being too ill for treatment.

Table 35: Counselling for treatment preparation and adherence

Step 1: Establish rapport and relationship of trust with the patient

- Provide necessary information and guidance
- Encourage peer participation and help identify treatment support persons
- Encourage disclosure
- Develop an ***individual treatment plan,*** fitting ART into the patient's lifestyle/daily events and identifying treatment reminders
- Assess patient's readiness for and commitment to ART. Readiness to commence ART may be assessed by:
  - past ability to attend clinic regularly and not miss appointments
  - past ability to take OI prophylaxis, such as cotrimoxazole
  - past ability to complete a full course of TB therapy
  - adequate understanding
- There should be strict adherence to treatment. ***Adherence to recommended regimens should be > 95% to avoid development of ARV drug resistance. This means that missing > 3 doses per month is associated with an increased risk of drug resistance and failure***
- If patients have difficulty in adhering to regular doses, reinforce adherence counselling. List barriers to adherence and develop strategies to overcome these barriers. Enlist community outreach teams and peer support groups of PLHA, as appropriate
- Treatment is lifelong
- The timing of drug intake is critical (e.g. drugs taken twice daily must be taken every 12 hours + one hour)
- Missed doses can be taken up to 6 hours later in a twice-daily regimen. If > 6 hours elapse, skip the dose and take next normal dose
- Dietary requirements with ARV drugs: Some drugs are taken with food, some on an empty stomach, and some require an increased intake of water
- The side-effects of the drugs have to be explained to and understood by the patient before commencing ART
- Give an ***information sheet*** to patients about the ART regimen they are taking. *See Annex 7*
- People on ART need to continue to use condoms regularly and practise safe injecting drug use

Table 35: Counselling for treatment preparation and adherence

- Other medications, including herbal/traditional products, may interact with ART. Patients need careful counselling about which medications are allowed and which are not with their ART
- Regular clinic attendance for monitoring of efficacy, side-effects and adherence is essential
- If patients cannot keep the appointment, they should call or a home visit should be made

Step 2: Counselling – in one or more individual sessions

- Help the patient explore his/her feelings. Many patients are preoccupied with problems related to family, job, relationships, etc. and cannot focus on strict adherence until negative feelings about these problems are sorted out
- Many have no private place to store their medicines and are not able to take them in privacy. Not wanting others to know their HIV status is by far the commonest reason for poor adherence by patients. Patients must be realistic about who to confide in about their HIV status and how to tell them
- Check for any financial difficulties the patient may be experiencing. Some patients may not follow up if they do not have money to travel to the centre, or their health may be affected by a poor diet. Help patients develop secondary support systems for themselves

Step 3: Solving practical problems and creating a treatment plan

- Where will the ARV drugs be stored?
- At what time will they be taken?
- How will the patient remember or who will remind him/her to take the medication if he/she forgets?
- What will the patient do if his/her normal routine is interrupted?
- A time should be agreed upon to meet or telephone the patient within a few days of starting ART to discuss any problems

Table 36: Checklist to assess treatment adherence

- Number of doses missed in the past 3 and 15 days
- Number of doses missed since the last visit
- Whether doses are taken at correct time (if not, ask about delay in hours/days)
- If correct dose is taken
- Reasons for missing/incorrect dosing/non-adherence
- Estimated proportion of doses taken using a visual analogue scale

The key to successful adherence is educating the patient before the initiation of therapy, supporting ARV initiation as the patient first starts taking medications, and continuously monitoring and supporting adherence. The reinforcement of the principles of adherence by treatment supporters (guardian), relatives, friends and community support personnel is of great help. Providing PLHA with an **information sheet on the ART regimen** they are taking will facilitate adherence and education. *See Annexes 7 and 8.*

Refer to HIV Counselling Training Modules for VCT, PPTCT and ART Counsellors, NACO 2006 for more details

A16 Section

Nutritional Aspects of HIV

16.1 In India, the HIV/AIDS epidemic is occurring in populations in which malnutrition is already endemic. Opportunistic infections and related syndromes, such as TB and diarrhoea, affect the nutritional status as well as physical factors such as appetite and weight.

Barriers to good nutrition include the following:

- Barriers related to information: provider barriers, client barriers, system barriers
- Barriers related to food choices: economic, geographical, physical, time constraints
- Barriers related to cooking and supplying: who will cook/supply
- Cultural, social and religious barriers: vegetarians
- Personal barriers: depression, loss of appetite, concurrent substance abuse, alcohol use

Depending upon the stage of the disease, HIV/AIDS produces

- Reduction in food intake
- Difficulties related to digestion
- Difficulties related to absorption
- Altered metabolism of nutrients (e.g. metabolism of carbohydrates/lipids may be different in HIV)
- Altered body functions: inability to produce saliva, other juices
- Improper utilization of fats

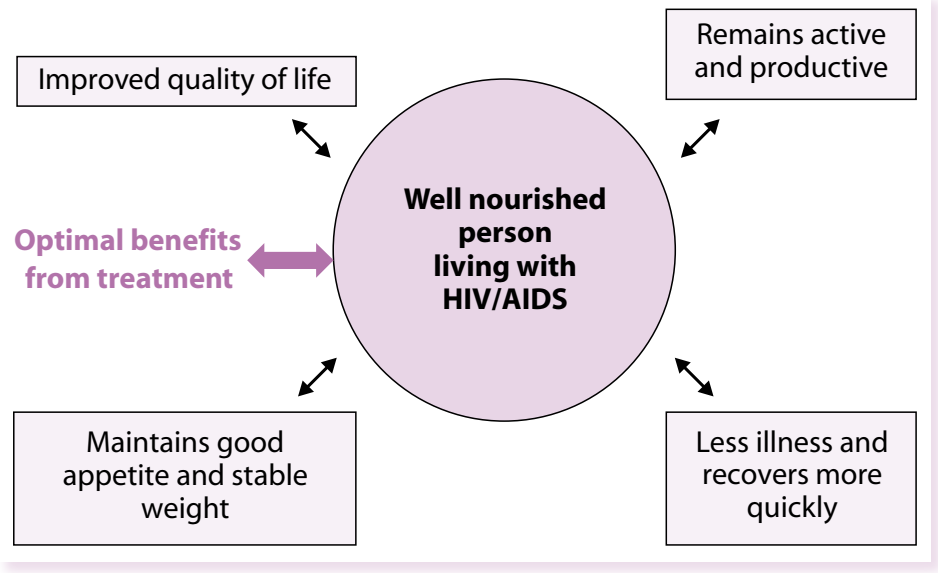
16.2 Increased Resting Energy Expenditure (REE) is Observed in HIV-infected Adults

- Energy requirements are likely to increase by 10% to maintain body weight and physical activity in asymptomatic HIV-infected adults, and maintain growth in asymptomatic children.
- During symptomatic HIV, and subsequently during AIDS, energy requirements increase by approximately 20–30% to maintain adult body weight.

Table 37: Relationship between HIV and malnutrition

Effect of malnutrition on HIV	Effect of good nutrition on HIV
Increased mouth ulcers, sores, etc., which facilitate transmission of infections	Reduced complications of HIV (diarrhoea, fever, muscle wasting, weight loss)
Reduced immunity to OIs, TB, pneumonia, etc.	Stronger immune system (proteins, antioxidants, zinc, selenium)
Rapid progression from HIV infection to AIDS	Maintenance of required body weight, improving energy level, productivity, sense of wellbeing
	Supports the effective action of OI treatment and ART
Nutrition is an investment that has both physical and psychological benefits.	

Effect of nutrition on HIV/AIDS



16.3 Nutritional counselling is necessary every time the PLHA visits the clinic. Give practical advice on nutrition to PLHA and their care-givers:

(1) Simple steps on food handling and safety:
- Cook food thoroughly.
- Eat cooked food immediately.
- Store food carefully.
- Re-heat cooked food thoroughly.
- Avoid contact between raw and cooked food.
- Wash your hands thoroughly before and after cooking.
- Keep kitchen surface clean.
- Protect food from rodents, insects and animals.
- Use clean water.

(2) Commonly available food items and their nutritional content (Table 37).

(3) Recommendations on which food items to avoid:
- Raw eggs
- Food that has not been thoroughly cooked, especially meat and chicken
- Unboiled water or juices made with unboiled water
- Alcohol and coffee
- Stale food

(4) Symptom-based nutritional care and support (Table 38)

(5) Nutrition and ART, including food–drug interactions

Paying greater attention to diet and nutrition may enhance the acceptability and effectiveness of ART, as well as adherence to it. Give counselling on correct nutrition and foods which can enhance the well-being of PLHA. Food can affect the absorption metabolism, distribution and excretion of medication. Medication too can affect the metabolism of food.

- High fat meals reduce the absorption of Indinavir (unboosted).
- High fat meals increase bioavailability of Tenofovir.
- Ritonavir causes changes in fat metabolism.
- The side-effects of medication may adversely affect the consumption and absorption of food, e.g. AZT causes nausea, anorexia and vomiting; didanosine causes vomiting, diarrhoea and dryness of mouth.

- The combination of certain medications and alcohol can produce side-effects, e.g. taking didanosine together with alcohol may result in pancreatitis.
- Take AZT with low-fat meals.
- Take didanosine on an empty stomach.
- Avoid alcohol with any medication.

Table 38: Commonly available food items and their nutritional content

Item	Nutritional value
Cereals	Carbohydrates, vitamin B
Pulses	Protein, vitamin B
Nuts and oil seed	Protein, energy, vitamin B
Fats and oil	Fat
Fruits and vegetables	Vitamins C, A, carbohydrates, iron and pectin
Roots and tubers	Carbohydrates, carotene, calcium and fibre
Milk and milk products	Protein, calcium, vitamin B
Flesh foods, e.g. meat	Protein, vitamin B, calcium and iron
Condiments and spices	Beta carotene and vitamin C
Salt	Helps maintain electrolyte balance
Fibre	**Soluble Fibre** • Helps people who have loose stools • Available in – fruit like apples, oranges, plums – vegetables like carrots, potatoes, – legumes and grains like kidney beans, soya, barley, oats, split peas
	Insoluble Fibre • Adds bulk to stool • Helps prevent constipation Found in whole grain cereals, brown rice, potatoes with skin, apples with skin, raisins, bananas
Special effects: • Garlic: contains Allicin, which has antibacterial, antiviral and antioxidant properties (2–3 cloves a day). • Turmeric: contains polyphenol compounds that have antioxidant properties and ability to fight inflammation.	

Table 39: Symptom-based nutritional care

Symptoms	Management
Loss of appetite	• Eat small, frequent meals (5—6 meals/day) • Eat nutritious snacks • Drink plenty of liquids • Take walks before meals—the fresh air helps to stimulate appetite • Have family or friends assist with food preparation • Take light exercise and do light activity • Add flavour to drink and food
Mouth ulcer	• Avoid citrus fruits and acidic and spicy foods • Eat food at room temperature • Eat soft and moist food • Avoid caffeine and alcohol
Candidiasis	• Eat soft, cool and bland foods (like rice porridge, oat meal, mashed vegetables, apple juice, milk)

Table 39: Symptom-based nutritional care	
	• Add garlic (optional) • Avoid sugar (glucose, cane sugar), yeast, caffeine, spicy food, carbonated drinks and alcohol
Nausea and vomiting	• Eat small, frequent meals • Avoid an empty stomach as this makes the nausea worse. • Eat bland food • Avoid food with strong or unpleasant odours • Drink plenty of liquids • Rest and relax after meals • Avoid lying down immediately after eating • Avoid coffee and alcohol
Constipation	• Eat fibre-rich food and sprouted food • Take light exercise and do light activity • Drink plenty of water • Take warm drinks
Anaemia	• Eat meat and fish • Eat cereals like *ragi* and *bajra* • Eat a variety of green leafy vegetables (radish greens, mint, *paruppu keerai/ kulfa kan*, cauliflower leaves and *sundaikai*). The best way for the body to utilize iron from plant sources is to combine food rich in iron with a food rich in vitamin C, like oranges, lemons, tomatoes and papaya. • Take jaggery and dates between meals

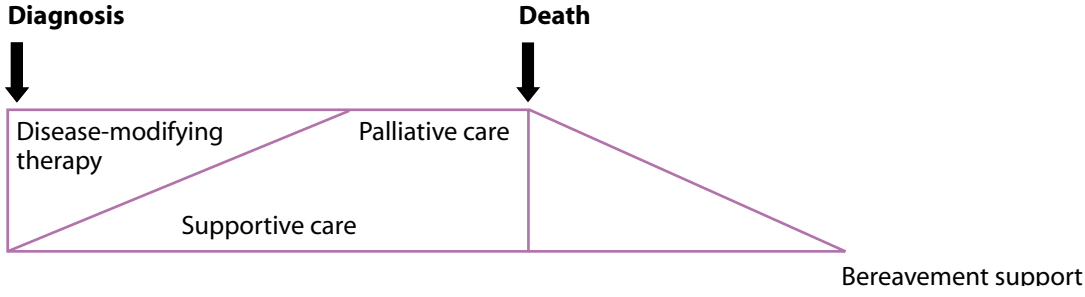
Table 40: Managing side effects the role of diet	
Side-effects	**Preferred diet**
Neuropathy – tingling and numbness	More vitamin B12 (fish, liver, poultry, dairy products)
Gas, bloated feeling, discomfort	Drink plenty of water May take curd Avoid pulses and legumes
Constipation	Drink plenty of water, high fibre, nuts, fruits, popcorn
Weakness, anaemia	Iron-rich food (beans, peas, dry fruits, dates, liver); food rich in folic acid and vitamin B12 (fortified cereals, orange juice, fish, liver, dairy products)

A17 Section

Palliative Care in HIV

17.1 The Government of India has adopted WHO's definition of palliative care, which is *the active total care of patients whose disease is not responsive to curative treatment* (*Manual on Palliative Care, MOHFW, November 2005*). Palliative care is an "approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual". Palliative care extends, if necessary, to support in bereavement.

Relationship between disease–modifying, supportive and palliative care



17.2 Palliative care in HIV:

- Is family and patient-centred
- Optimizes the quality of life by active participation, prevention and treatment of suffering
- Involves an inter-disciplinary team approach throughout the continuum of illness, placing critical importance on the building of respectful and trusting relationships
- Addresses physical, intellectual, emotional, social and spiritual needs

The availability of ART and palliative care has made HIV a chronic, manageable disease for many. Apart from regular pain management, nutritional support and OI management, palliative care includes giving support for drug failure and severe toxicities due to ART.

Special attention needs to be given to the following HIV-related conditions, which may present as terminal illness. These conditions can be managed with proper medical care and support.

1. Severe oral and oesophageal candidiasis, leading to severe pain and weight loss
2. Cryptococcal meningitis and Toxoplasma encephalitis.

17.3 The Main Components of Palliative Care Include

- Pain management.
- Symptom management
- Nutritional support
- Psychosocial support
- Spiritual support
- End-of-life care
- Bereavement counselling

17.3.1 Management of Pain

Step 1: Assess the patient for pain

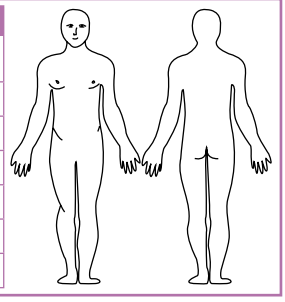
- Determine the severity, site and nature of the pain (bone pain, mouth pain, shooting nerve pain, colicky pain, severe muscle spasms).
- If there is infection, prompt management of infection is the main step in controlling the pain (e.g. treating severe oral and oesophageal candidiasis with fluconazole relieves the pain).
- The severity of the pain can be graded with the help of the tools below.

GO BY WHAT THE PATIENT SAYS IS HURTING: Do not disregard the patient's complaint of pain just because there is no apparent physical cause.

Pain can be assessed using the PQRST characteristics	
P - Palliative factors Provocative factors	'What makes it better?' What makes it worse?'
Q - Quality	'What exactly is it like?'
R - Radiation	'Does it spread anywhere?'
S - Severity	'How severe is it?' 'How much does it affect your life?'
T - Temporal factors	'Is it there all the time or does it come and go?' 'Is it worse at any particular time of the day of night

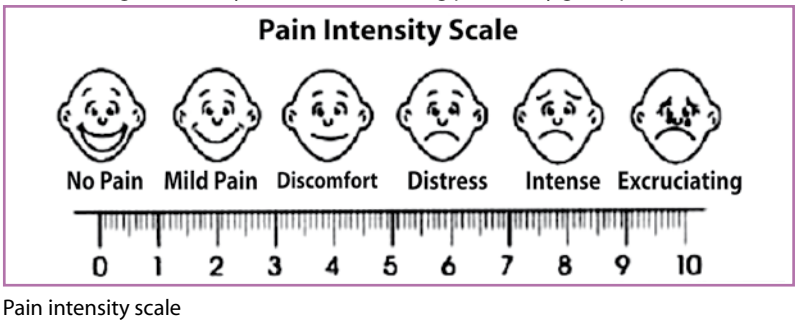
PQRST Characteristics

Pain Assement						
Pain site	Palliative factors	Provocative Factors	Quality of pain	Radiation	Severity	Temporal factors



Various scales for pain assessment are	
• Descriptive Scale • Numeric Scale • Visual analogue Scale	• Percentage Scale • Coin Scale • Face Scale

The following format may be used for assessing pain in any given patient.



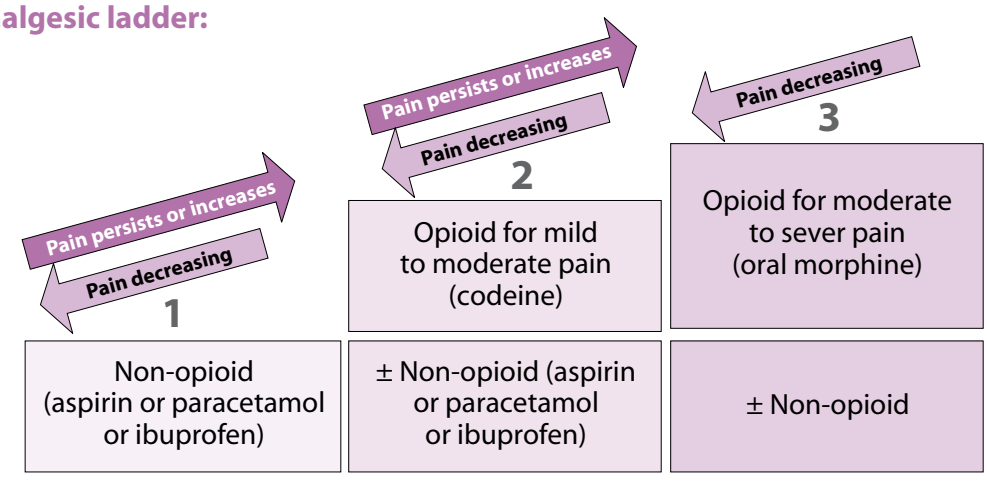
Pain intensity scale

Step 2: Decide the treatment strategies for pain

Table 41: Strategies for treatment of pain

By mouth	By the clock
• If possible, administer painkiller by mouth (rectal administration is an alternative—avoid intramuscular route).	• Give painkillers at fixed time intervals (by clock or radio or sun). • Start with a small dose, then titrate the dose against the patient's pain, until the patient is comfortable. • The next dose should be given before the effect of the previous one wears off. • For breakthrough pain, give an extra "rescue" dose, in addition to the regular schedule.

By the analgesic ladder:



The right dose is the dose that relieves the patient's pain.

Step 3: Prescribe analgesics – use of opioid and non-opioid

Give only one drug from the opioid and non-opioid groups at a time. The exception is if codeine cannot be given, use aspirin every four hours combined with paracetamol every four hours—overlap so one is given every two hours.

Table 42: Use of analgesics in pain relief

	Analgesics	Starting dose in adults	Range	Side effects/cautions
STEP 1	**Non-opioid**			
	Paracetamol (also lowers fever)	2 tablets of 500 mg every 4–6 hours (skip dose at night or give another analgesic to keep total to 8 tablets)	Only 1 tablet may be required in elderly or very ill, or when combined with opioid. Mild pain might be controlled with 6 hourly dosing	Do not exceed eight 500 mg tablets in 24 hours (more can cause serious liver toxicity)
	Aspirin (acetylsalicylic acid) (also anti-inflammatory and lowers fever)	600 mg (2 tablets of 300 mg) every 4 hours		Avoid use if gastric problems. Stop if epigastric pain, indigestion, black stools petechiae or bleeding Avoid if presence of any bleeding
	Ibuprofen (also anti-inflammatory, lowers fever, for bone pain)	400 mg every 6 hours		Max. 8 tablets per day

STEP 2	**Opioid for mild to moderate pain (give in addition to aspirin or paracetamol)**			
	Codeine (if not available, consider alternating aspirin and paracetamol*)	30 mg every 4 hours	30–60 mg every 4 to 8 hrs. Maximum daily dose for pain 180–240 mg due to constipation—switch to morphine	Give laxative to avoid constipation unless diarrhoea
STEP 3	**Opioid for moderate to severe pain**			
	Oral morphine 5 mg/5 ml or 50 mg/5 ml. Drop into mouth. Can also be given rectally (by syringe)	2.5–5 mg every 4 hours (dose can be increased by 1.5 or doubled after 24 hours if pain persists)	According to need of patient and breathing. There is NO ceiling dose	Give laxative to avoid constipation unless diarrhoea

17.3.2 Give medications to control special pain problems

There are nerve injury pains and pains from special conditions which can be relieved by specific medications. Provide specific treatment in combination with drugs from the analgesic ladder.

Table 43: Medications for special pain problems

Special pain problems	Medication—adolescent/adult
For burning pains; abnormal sensation pains; severe, shooting pains with relatively little pain in between; pins and needles	Low dose amitriptyline (25 mg at night or 12.5 mg twice daily; some start 12.5 mg daily)—wait 2 weeks for response, then increase gradually to 50 mg at night or 25 mg twice daily
For muscle spasms in end-of-life care or paralyzed patient	Diazepam 5 mg orally or rectally 2–3 times per day
Herpes zoster (or the shooting pain following it) Refer patients with ophthalmic zoster	Low dose amitriptyline Early eruption: aciclovir if available; apply gentian violet if ruptured vesicles
Gastrointestinal pain from colic only after intestinal obstruction has been excluded (ie. vomiting, no stool and gas passing, visible bowel movements)	Codeine 30 mg every 4 hours or Hyoscine 10 mg three times daily (can increase up to 40 mg three times daily)
Bone pain or renal colic or dysmenorrhoea	Ibuprofen (or other NSAID)
If pain from: • Swelling around tumour • Severe esophageal ulceration and cannot swallow • Nerve or spinal cord compression • Persistent severe headache (likely from increased intracranial pressure)	When giving end-of-life care and referral not desired, can consider use of steroids under careful clinical supervision

17.3.3 Additional methods for pain control

Combine these with pain medications if patient agrees and it helps:

- Emotional support.
- Physical methods: Touch (stroking, massage, rocking, vibration). Ice or heat. Deep breathing
- Cognitive methods: distraction such as radio, music, imagining a pleasant scene.
- Prayer (with respect to patient's practice).
- Traditional practices which are helpful and not harmful—get to know what can help in the local setting.

17.3.4 Symptom Management

Table 44: Management of symptoms with medications and home care

Symptoms	Medications to give	Home care
Nausea and Vomiting:	Give Anti-emetic: metoclopromide (10 mg every 8 hours). Give only for a day at a time or haloperidol (1–2 mg once daily) or chlorpromazine (25–50mg every 6–12 hours).	• Eat small, frequent meals • Avoid an empty stomach as this makes the nausea worse • Eat bland foods • Avoid foods with strong or unpleasant odours. • Drink plenty of liquids. • Rest and relax after and between meals. • Avoid lying down immediately after eating. • Avoid coffee and alcohol.
Painful mouth ulcers or pain on swallowing:	• If Candida: give fluconazole, nystatin or miconazole orally. Topical anesthetics can provide some relief. Pain medication may be required according to analgesic ladder • For Aphthous ulcers: crush one 5 mg prednisone tablet and apply a few grains. • Smelly mouth/breath (halitosis) from oral cancer or other lesions: metronidazole 400mg bd or chlorhexidine Gluconate 1% 10 ml qid mouthwash or hexetidine 0.1% 10 ml qid or Benzydamine 0.5% mouth wash or sodium bicarbonate mouthwash (1 tsp in 1 pint warm water) • For Herpes simplex: 5 ml nystatin solution (500,000 U) + 2 tablets metronidazole + 1 capsule aciclovir (if available)—paint on lesions.	• Remove bits of food stuck in the mouth with cotton wool, gauze or soft cloth soaked in salt water. • Rinse the mouth with diluted salt water (a finger pinch of salt or 1/2 teaspoon sodium bicarbonate in a glass of water) after eating and at bedtime. • Mix 2 tablets of aspirin in water and rinse the mouth up to 4 times a day. • Soft diet to decrease discomfort such as rice porridge, oat meals, depending on what the sick person feels is helpful. • More textured foods and fluids may be swallowed more easily than fluids. • Avoid extremely hot or cold or spicy foods.
Hiccups:	• First try maneuvers to control. If oral thrush, treat. • If no response or recurrent: metoclopromide (10 mg tablet, 1–2 tablets three or four times daily). OR - haloperidol (5 mg tablet: 1/4 to 1/2 tablets once to three times daily). • If patient has brain tumor, consider anti-epileptic medication.	• Maneuvers to stop hiccups: • Stimulate the throat: • Quickly eat 2 heaped teaspoons sugar, or • Drink cold water or eat crushed ice, or Rub with a clean cloth inside the top of the mouth (feel toward the back, where the top of the mouth is soft). • Interrupt the normal breathing by: – Hold breath or breathe into paper bag—stop when you feel uncomfortable. – Pull knees to chest and lean forward (compress the chest).
Bed Sores:	• All patients need skin care to avoid pressure problems • Check for signs of infection. • For smelly tumours or ulcers, sprinkle metronidazole powder —enough to cover the area and keep dry.	• For small sores, clean gently with salt water and allow to dry. • Apply honey to bedsores that are not deep and leave the wound open to the air. • If painful, give painkillers such as paracetamol or aspirin regularly. • For deep or large sores, every day clean gently with diluted salt water, fill the bedsore area with pure honey and cover with a clean light dressing to encourage healing.

17.4 End-of-life Care

" How people die lives on the memory of those left behind"

The terminal phase is defined as the period when day-to-day deterioration, particularly of strength, appetite and awareness are occurring. Is it difficult to predict when death will occur and it is better not to do so. The aim of care at this stage should be to ensure the patient's comfort holistically, and a peaceful and dignified death.

Provide psychosocial and spiritual support to the patient:

- Other patients active listening, counseling and social/emotional support
- Spiritual support is very important:
  - Be prepared to discuss all matters if patient would like to.
  - Learn to listen with empathy.
  - Understand reactions to the losses in their life (the different stages of grief).
  - Be prepared to "absorb" some reactions, for example anger projected onto the health care provider
  - Do not impose your own views.
  - Share religious beliefs with the appropriate person (e.g. religious leader, spiritual counselor etc.) as required
- Empower the family to provide care: *see table 45*
  - Help the family come to terms with the fact that the patient is leaving them soon: let family members be around to see and talk to the patient
  - Deal with their anxieties and fears gently
  - Give information and skills.

Table 45: Management of end-of-life care issues

Steps	Actions
Preparing for death	• Encourage communication within family • Discuss worrying issues such as custody of children, family support, future school fees, old quarrels, funeral costs • Tell the patient that they are loved and will be remembered • Talk about death if the patient wishes to (keep in mind cultural taboos if not in a close relationship) • Make sure the patient gets help with feelings of guilt or regret • Connect with spiritual counselor or pastoral care as patient wishes
Presence	• Approach, be present with compassion • Outreach visit regularly with home-based care • Someone needs to hold hand, listen, converse with the patient and family. This could be a volunteer, NGO worker, outreach worker, counselor etc
Caring	• Provide comfort and physical contact by light touch, holding hands (if appropriate)
Comfort measures near the end of life	• Moisten lips, mouth, eyes • Keep the patient clean and dry and prepare for incontinence of bowel and bladder • Only give essential medications—pain relief, antidiarrhoeals, treat fever and pain (eg paracetamol round-the-clock) etc • Control symptoms with medical treatment as needed to relieve suffering (including antibiotics and anti-fungals, especially in HIV/AIDS) • Eating less is OK. Ensure hydration • Skin care/turning every 2 hours or more frequently to prevent bed sores • Make sure pain is controlled
Signs of imminent death	• Decreased social interaction—sleeps more, acts confused, coma • Decreased food and fluid intake—no hunger or thirst • Changes in elimination—reduced urine and bowel movements, incontinence • Respiratory changes—irregular breathing, "death rattle" • Circulatory changes—cold and grayish or purple extremities, decreased heart rate and blood pressure
Signs of death	• Breathing stops completely • Heart beat and pulse stop • Totally unresponsive to shaking, shouting • Eyes fixed in one direction, eyelids open or closed • Changes in skin tone—white to gray

A18 Section

NACO Standardized Reporting and Recording System

The National ART Programme is using a paper-based as well as computerized monitoring system consisting of registers, records and forms. The purpose of maintaining various registers and forms is to record relevant information in an easily retrievable manner and for different purposes. All centres are provided with a computer, a data manager and a broadband internet connection for this purpose. In the long term, NACO may shift to a fully electronic system, wherein ART data will be fed into the CMIS at the state, district or even ART center level. The standardized recording and reporting tools used for data collection and supervision includes:

Care and Treatment Records	
1.	Pre-ART Register
2.	ART Enrollment Register
3.	Patient Treatment Record
4.	Patient ID Card
Drug Dispensing and Stock Management Registers	
5.	Antiretroviral Drug Dispensing Register
6.	Antiretroviral Drug Stock Register
Programme Performance Monitoring Reports	
7.	Monthly ART Centre Report
8.	Quarterly ART Reports (Quarterly Antiretroviral Treatment Report Intersectoral Partners/NGOs/Private Hospitals and Quarterly Antiretroviral Treatment Report/Private Practitioners)
9.	Cohort Analysis Report
Supervision, Quality Assurance and Feedback Forms	
10.	ART Treatment Centre Appraisal Form
11.	ART Centres Supervisory Checklist

Refer to the National Operational Guidelines for ART centers 2007 for more details

B

Section

MANAGEMENT *of* OCCUPATIONAL EXPOSURE *Including* POST-EXPOSURE PROPHYLAXIS

B Section

Management of Occupational Exposure Including Post-exposure Prophylaxis

Avoiding occupational blood exposures is the primary way to prevent transmission of HIV, hepatitis B, and hepatitis C in health care settings. However, hepatitis B immunization and appropriate post-exposure management are integral components of a complete program to prevent infection following blood-borne exposure.

Appropriate post exposure management guidelines form an important element of work place safety. These guidelines describe the risks of infection, the preventive measures and the procedures to follow after occupational exposure.

This document is intended for medical doctors and is meant to assist in deciding when and how the post-exposure prophylaxis should be applied.

These guidelines will address the following aspects of occupational exposure to blood :

- Who is at risk?
- What is the risk?
- What practices may influence this risk and how to minimise the risk?
- What is the role of antiretroviral agents in reducing this risk?
- Issues about safety of PEP drugs and their use in pregnancy
- Operational recommendations to develop a comprehensive programme for PEP implementation with 24 hour access to needed drugs

This guideline has been prepared after the recommendations from the Experts Group Meeting to revise existing NACO guidelines, 3 Feb 2006. The recommendations are largely inspired by the guidelines formulated by the US Public Health Services. The guidelines will be updated regularly based on current evidence and global literature.

(CDC. Public Health Service guidelines for management of health-care worker exposures to HIV and recommendations for post exposure prophylaxis. MMWR. September 30, 2005/54 (RR09);1–17).

B1 Section

Definitions

Occupational exposure refers to exposure to potential blood-borne infections (HIV, HBV and HCV) that occurs during performance of job duties.

Non-occupational exposure refers to exposure to potential blood-borne infections (HIV, HBV, HCV) outside of the work setting.

Post exposure prophylaxis (PEP) refers to the comprehensive management given to minimize the risk of infection following potential exposure to blood-borne pathogens (HIV, HBV, HCV). This includes counseling, risk assessment, relevant laboratory investigations based on informed consent of the source and exposed person, first aid and depending on the risk assessment, the provision of short term (4 weeks) of antiretroviral drugs, with follow up and support.

The term **"Health Care Personnel (HCP)"** is defined as any persons, paid or unpaid; working in health-care settings who are potentially exposed to infectious materials (e.g. blood, tissue, and specific body fluids and medical supplies, equipment, or environmental surfaces contaminated with these substances). HCP include: emergency care providers, laboratory personnel, autopsy personnel, hospital employees, medical and nursing students and health care professionals of all levels. If required, PEP can also be given to public safety workers, including law enforcement personnel, prison staff, fire-fighters, workers in needle exchange programs and workers in international HIV programs.

"Exposure" which may place an HCP at risk of blood-borne infection is defined as:

- a percutaneous injury (e.g. needle-stick or cut with a sharp instrument),
- contact with the mucous membranes of the eye or mouth,
- contact with non-intact skin (particularly when the exposed skin is chapped, abraided, or afflicted with dermatitis), or
- contact with intact skin when the duration of contact is prolonged (e.g. several minutes or more) with blood or other potentially infectious body fluids.[4]

B2 Section

Principles of Providing PEP

Non-discrimination: The decisions about whether to provide PEP should be based on clinical consideration of risk only. Providers should give information, services and education without discrimination.

Confidentiality: The provision of information regarding PEP should be confidential including information about HIV testing, PEP provision and the reasons for seeking PEP.

Informed consent: for taking PEP needs to be obtained as for any other medical procedure. This should be written (*see annex 3*). Consent for HIV testing in context of HIV exposure and/or taking PEP , needs to be done according to national counseling and testing guidelines.

In special situations where the individual has limited/no capacity to consent (eg children, or unconscious or mentally ill adults), a proxy may be able to provide consent eg. parents/guardian/caretaker.

B3 Section

Who is at Risk?

Professionals with frequent blood exposures:

- Interns and medical students
- Nursing staff and students
- Physicians
- Surgeons
- Emergency care providers
- Dentists
- Labour and delivery room personnel
- Laboratory technicians
- Health facility cleaning staff and clinical waste handlers

Table 46: Potentially infectious body fluids

Exposure to body fluids considered '*at risk*'	Exposure to body fluids considered '*not at risk*'	
Blood Semen Vaginal secretions Cerebrospinal fluid Synovial, pleural, peritoneal, pericardial fluid Amniotic fluid Other body fluids contaminated with visible blood	Tears sweat Urine and faeces saliva	*unless these secretions contain visible blood*

Any direct contact (i.e., contact without barrier protection) to concentrated virus in a research laboratory or production facility requires clinical evaluation. For human bites, clinical evaluation must include the possibility that both the person bitten and the person who inflicted the bite were exposed to blood-borne pathogens. Transmission of HIV infection after human bites has been rarely reported.

B4 Section

What is the Average Risk of Acquiring HIV, Hep B or Hep C Infection after an Occupational Exposure?

The average risk of acquiring HIV infection after different types of occupational exposure is low compared to risk of infection with HBV or HCV. In terms of occupational exposure the important routes are needle stick exposure (0.3% risk for HIV, 9–30% for HBV and 1–10% for HCV) and mucous membrane exposure (0.09% for HIV).

Table 47: HIV transmission risk of different routes

Exposure route	HIV
Blood transfusion	90–95%
Perinatal	20–40%
Sexual intercourse	0.1 to 10%
Vaginal	0.05–0.1%
Anal	0.065–0.5%
Oral	0.005–0.01%
Injecting drugs use	0.67%
Needle stick exposure	0.3%
Mucous membrane splash to eye, oro-nasal	0.09%

Note: Needle-stick exposure for HBV is 9–30% and for HCV is 1–10%

Figure 1: How needle stick injuries occur

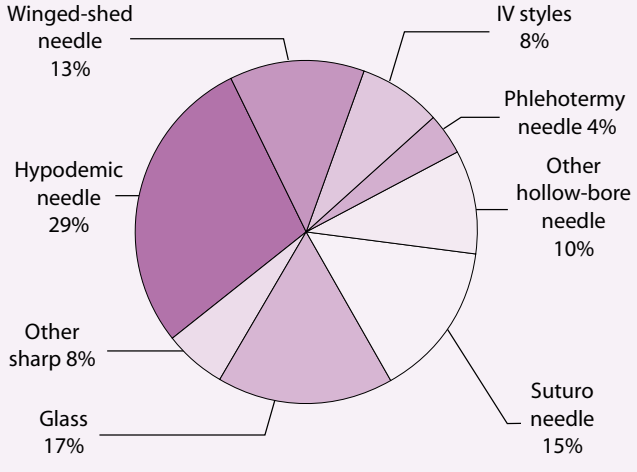
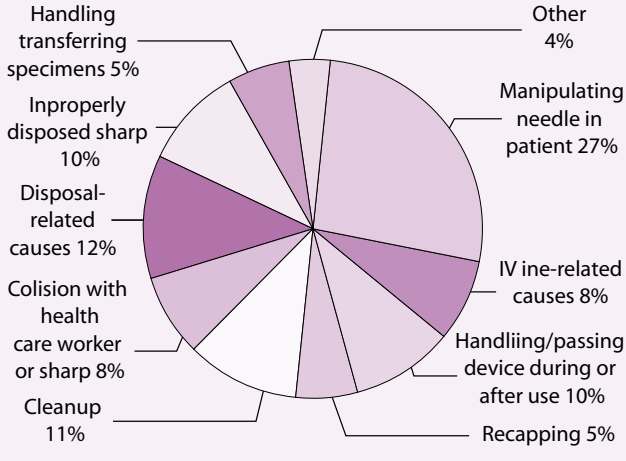


Figure 2: Activities associated with needle stick injuries



Figures 1 and 2 demonstrate how needle-stick injuries occur and the various activities associated with needle-stick injuries (CDC)

B5 Section

Practices that Influence Risk and How to Reduce Risk to Occupational Exposure

Certain work practices increase the risk of needlestick injury such as:

- Recapping needles (Most important).
- Transferring a body fluid between containers.
- Failing to dispose of used needles properly in puncture-resistant sharps containers.
- Poor healthcare waste management practices

How to protect oneself from needlestick/sharps injuries:

- Avoid the use of needles where safe and effective alternatives are available.
- Avoid recapping needles.
- Plan for safe handling and disposal of needles before using them.
- Promptly dispose of used needles in appropriate sharps disposal containers.
- Report all needle stick and sharps-related injuries promptly to ensure that you receive appropriate follow-up care.
- Participate in training related to infection prevention.
- Help your institute select and evaluate devices with safety features that reduce the risk of needle stick injury.
- Use devices with safety features provided by the institute (wherever possible).
- Record and monitor injuries with an injury register in each location of healthcare setting.

Performing these activities in a rush increases the likelihood of an accidental exposure

B6 Section

Preventing Exposure to and Transmission of HIV and other Viruses

Staff Information: All categories of HCP within the hospital should be informed about how to protect themselves against HIV and other pathogens transmitted by blood or body fluids. The information must be reinforced on a regular basis. All staff share an individual and collective responsibility in this regard. The Medical Superintendent (MS)/Dean/Principal/In-charge of the Hospital must constitute a hospital infection control committee which will conduct regular trainings and monitor hospital infection control including universal precaution and post-exposure prophylaxis implementation and quality control. The MS must ensure that the hospital has a written protocol and Standard Operational Procedures (SOP) to handle occupational exposure and that these are disseminated to all relevant personnel/departments.

The Medical Superintendent of the hospital has the responsibility of informing all staff about:

- the universal precautions to be followed in health services (*see table 48*).
- use of personal protective equipment.
- other preventive measures to be taken against these viruses (including vaccination).
- SOPs to be followed in case of accidental exposure to blood and body fluids.

All hospital staff must know whom to report for PEP in case of occupational exposure

Minimise the use of sharps/injections: All medical staff should try to minimize the use of invasive interventions for example — to use oral drugs in place of injections wherever possible. Where the use of sharps is indicated to try to use safer alternatives where practical and possible within the limitations of the system.

Protection against hepatitis B and C: All HCP should be vaccinated against the hepatitis B virus. The vaccination for Hepatitis B consists of 3 doses: initial, 1 month, and 6 months. Most (99%) seroconvert after completing the full course. There is no vaccine or prophylaxis available against hepatitis C.

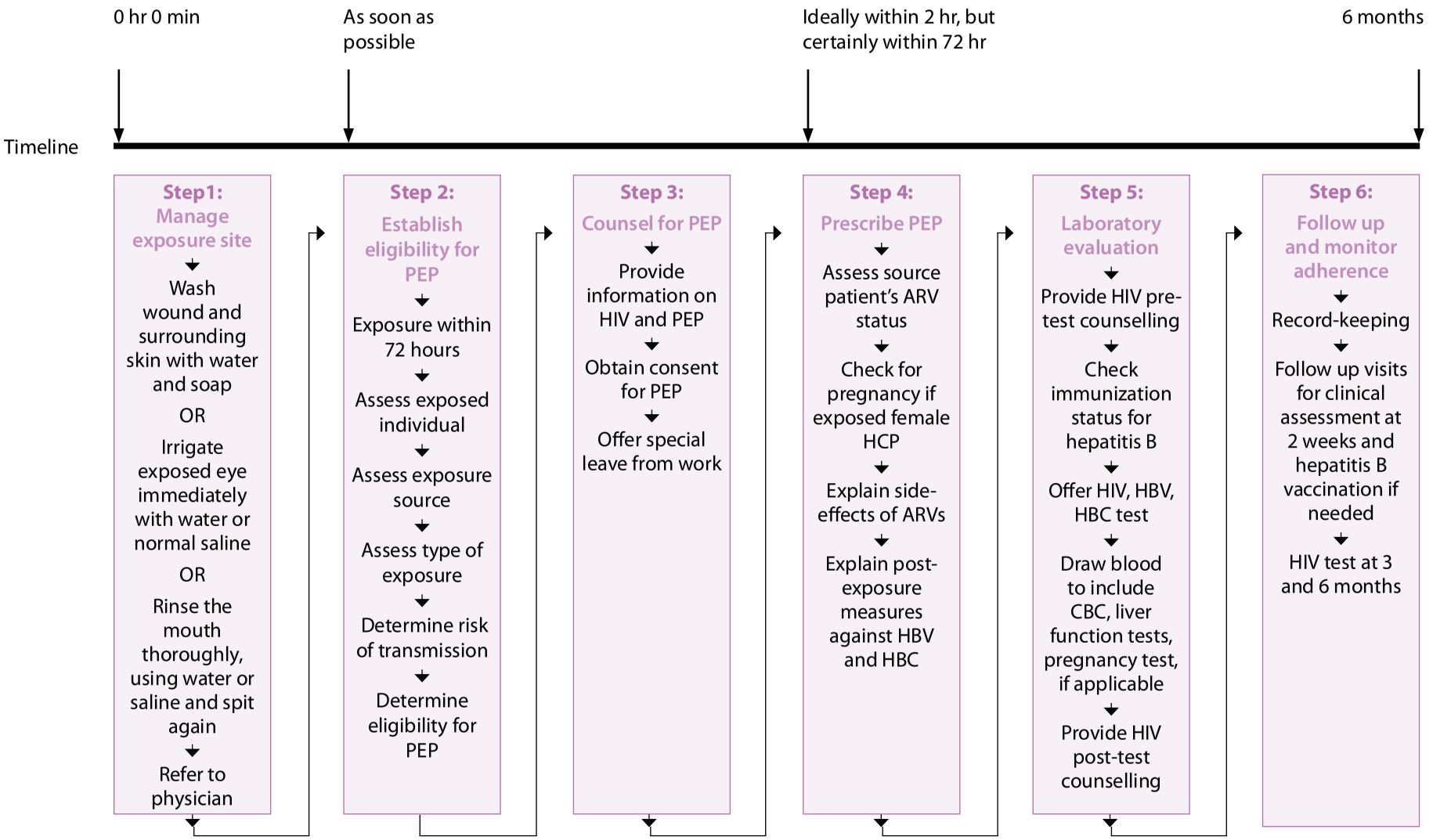
Table 48: Universal precautions

Universal precautions are intended to prevent the exposure of health-care workers and patients to blood-borne pathogens. These must be practised in regard to the blood and body fluids of all patients, regardless of their infection status.

Universal precautions include:

- hand-washing before and after all medical procedures
- safe handling and immediate safe disposal of sharps: not recapping needles; using special containers for sharp disposals; using needle cutter/destroyers; using forceps instead of fingers for guiding sutures; using Vacutainers where possible
- safe decontamination of instruments;
- use of protective barriers whenever indicated to prevent direct contact with blood and body fluid such as gloves, masks, goggles, aprons, and boots. A HCP who has a cut or abrasion should cover the wound before providing care
- safe disposal of contaminated waste

Steps for managing occupational exposure



See annex 10: Occupational exposure management- sample flow chart

B7 Section

Management of the Exposed Person

7.1 Step 1: Management of Exposure Site–First Aid

For skin—if the skin is broken after a needle-stick or sharp instrument:

- Immediately wash the wound and surrounding skin with water and soap, and rinse. Do not scrub.
- Do not use antiseptics or skin washes (bleach, chlorine, alcohol, betadine).

After a splash of blood or body fluids:

- To unbroken skin:
  - Wash the area immediately
  - Do not use antiseptics
- For the eye:
  - Irrigate exposed eye immediately with water or normal saline
  - Sit in a chair, tilt head back and ask a colleague to gently pour water or normal saline over the eye.
  - If wearing contact lens, leave them in place while irrigating, as they form a barrier over the eye and will help protect it. Once the eye is cleaned, remove the contact lens and clean them in the normal manner. This will make them safe to wear again
  - Do not use soap or disinfectant on the eye.
- For mouth:
  - Spit fluid out immediately
  - Rinse the mouth thoroughly, using water or saline and spit again. Repeat this process several times
  - Do not use soap or disinfectant in the mouth

Consult the designated physician of the institution for management of the exposure immediately.

Table 49: Summary of do's and don't

Do	Do Not
Remove gloves, if appropriate	**Do not** panic
Wash the exposed site thoroughly with running water	**Do not** put the pricked finger in mouth
Irrigate with water or saline if eyes or mouth have been exposed	**Do not** squeeze the wound to bleed it
Wash the skin with soap and water	**Do not** use bleach, chlorine, alcohol, betadine, iodine or other antiseptics/detergents on the wound
** Do - Consult the designated physician immediately as per institutional guidelines for management of the occupational exposure **	

7.2 Step 2: Establish eligibility for PEP

The HIV sero-conversion rate of 0.3% after an AEB (for percutaneous exposure) is an average rate. The real risk of transmission depends on the amount of HIV transmitted (= amount of contaminated fluid and the viral load).

A designated person/trained doctor must assess the risk of HIV and HBV transmission following an AEB. This evaluation must **be made rapidly**, so as to start any treatment as soon as possible after the accident (Ideally within 2 hours but certainly within 72 hours). This assessment must be made thoroughly (because not every AEB requires prophylactic treatment).

The first dose of PEP should be administered within the first 72 hours of exposure and the risk evaluated as soon as possible. If the risk is insignificant, PEP could be discontinued, if already commenced.

PEP must be initiated as soon as possible, preferably within 2 hours

Two main factors determine the risk of infection: the nature of exposure and the status of the source patient.

7.2.1 Assessing the nature of exposure and risk of transmission

Three categories of exposure can be described based on the amount of blood/fluid involved and the entry port. These categories are intended to help in assessing the severity of the exposure but may not cover all possibilities.

Table 50: Categories of exposure

Category	Definition and example
Mild exposure :	mucous membrane/non-intact skin with small volumes E.g. : a superficial wound (erosion of the epidermis) with a plain or low calibre needle, or contact with the eyes or mucous membranes, subcutaneous injections following small-bore needles
Moderate exposure:	mucous membrane/non intact skin with large volumes **OR** percutaneous superficial exposure with solid needle E.g. : a cut or needle stick injury penetrating gloves
Severe exposure :	percutaneous with large volume e.g. : • an accident with a high calibre needle (≥18 G) visibly contaminated with blood; • a deep wound (haemorrhagic wound and/or very painful); • transmission of a significant volume of blood; • an accident with material that has previously been used intravenously or intra-arterially.

The wearing of gloves during any of these accidents constitutes a protective factor.

Note : In case of an AEB with material such as discarded sharps/needles, contaminated for over 48 hours, the risk of infection becomes negligible for HIV, but still remains significant for HBV. HBV survives longer than HIV outside the body.

7.2.2 Assessing the HIV status of the source of exposure

PEP needs to be started as soon as possible after the exposure and within 72 hours. In animal studies, initiating PEP within 12, 24 or 36 hours of exposure was more effective than initiating PEP 48 hours or 72 hours following exposure. PEP is not effective when given more than 72 hours after exposure. A baseline **rapid HIV testing** should be done before starting PEP.

Initiation of PEP where indicated should not be delayed while waiting for the results of HIV testing of the source of exposure. Informed consent should be obtained before testing of the source as per national HIV testing guidelines.

Table 51: Categories of situations depending on results of the source	
Source HIV Status	**Definition of risk in source**
HIV negative	Source is not HIV infected but consider HBV and HCV
Low risk	HIV positive and clinically asymptomatic
High risk	HIV positive and clinically symptomatic (see WHO clinical staging)
Unknown	Status of the patient is unknown, and neither the patient nor his/her blood is available for testing (e.g. injury during medical waste management the source patient might be unknown). The risk assessment will be based only upon the exposure **(HIV prevalence in the locality can be considered)**
Refer to annex 15: Risk assessment for the source person	

HIV infection is not detected during the primary infection period by routine-use HIV tests. During the "window period", which lasts for approximately 6 weeks, the antibody level is still too low for detection – but infected persons can still have a high viral load. This implies that a positive HIV test result can help in taking the decision to start PEP, but **a negative test result does not exclude HIV infection**. In districts or some population groups with a high HIV prevalence, a higher proportion of HIV-infected individuals are found in the window period. In these situations, a negative result has even less value for decision-making on PEP.

7.2.3 Assessment of the exposed individual

The exposed individual should have confidential counselling and assessment by an experience physician. The exposed individual should be assessed for **pre-existing HIV infection** (*see Step 5*) intended for people who are HIV negative at the time of their potential exposure to HIV. Exposed individuals who are known or discovered to be HIV positive should not receive PEP. They should be offered counselling and information on prevention of transmission and referred to clinical and laboratory assessment to determine eligibility for antiretroviral therapy (ART). Besides the medical assessment, **counselling** (*see Step 3*) exposed HCP is essential to allay fear and start PEP (if required) at the earliest.

7.3 Step 3: Counseling for PEP

Exposed persons (clients) should receive appropriate information about what PEP is about and the risk and benefits of PEP in order to provide informed consent. It should be clear that PEP is not mandatory.

Table 52: Key information to provide informed consent to the client after occupational exposure	
Key information to exposed person (client)	**Specific Details include**
• The risk of acquiring HIV infection from the specific exposure	• Ask client for understanding of HIV transmission risk after exposure • The risk of getting HIV infection from a person known to be HIV positive is estimated to be - Sharps injury: 3 in 1000 exposures (0.3%) - Mucous membrane splash: 1 in 1000 exposures (0.1%) - the risk in increased with large exposure eg needle-stick from hollow bore needles with visible blood, from artery or vein and from source patients with high viral load (usually very sick persons with OIs)
• What is known about PEP efficacy	• Ask client's understanding of PEP • PEP is provided to prevent potential transmission of the HIV virus • PEP is not 100% effective and should be given within 72 hours (ideally as soon as possible, if eligible). • Balance risk and benefits of PEP: PEP *may* prevent HIV transmission, versus possible risk of side effects

Table 52: Key information to provide informed consent to the client after occupational exposure	
• Information about client's risk of HIV infection based upon a risk assessment (if s/he has not had a recent HIV test) • The importance of being tested and receiving appropriate post-test counselling (although HIV testing can be delayed if needed) • That PEP medicines will be discontinued if their initial (baseline) HIV test is positive	• Client's possibility of prior HIV infection should be assessed • Counsel for HIV testing and follow-up psychosocial support – where possible rapid testing should be used based on national testing guidelines • Inform if the baseline HIV test is positive, then the PEP will be discontinued • Arrange referral to ART centers for assessment if found HIV positive
• Importance of adhering to medication once started • Duration of the course of medicine (4 weeks)	• Discuss dosing of the PEP medicine eg pill should be taken twice a day for 28 days, once in the morning and once in the evening • Depending on the nature and risk of exposure, 2 drugs or 3 drugs may be used • Side effects may be important with use of 3 drugs • Expert opinion/consultation by phone or referral may be needed with a HIV specialist if 3rd drug is to be used • Arrange for special leave from work (2 weeks initially)
• Common side effects that may be experienced	• Discuss possible side effects of the PEP medicines eg. nausea, fatigue, headache (depending on which drugs given) • Side effects often improve over time. It is often minor and do not need specialised supervision • Symptomatic relief can also be given by using other drugs
• That they can stop at any time but will not get the benefit of PEP – if the source is HIV positive	• Animal studies suggest that taking less than 4 weeks of PEP does not work • If client decides to stop at any time, s/he needs to contact the physician before stopping the medications • Arrange for follow-up visit and decide further course of action/follow-up
• Prevention during the PEP period eg sexual intercourse and unplanned pregnancy	• After any AEB, the exposed person should not have unprotected sexual intercourse until it is confirmed, 3 months after the exposure, that s/he is not HIV infected. • It is also advised to avoid pregnancy • Use of condoms is essential
• If client is pregnant – she can still take PEP during pregnancy	• The PEP drugs used are safe for pregnancy • If the client gets HIV during the pregnancy due to the exposure, the baby will have some risk of becoming HIV infected
• Safety of PEP if the client is breastfeeding	• The PEP drugs used are safe during breast-feeding • May consider stopping breastfeeding if PEP is indicated.
• Educate client on the possible signs and symptoms of early HIV sero-conversion	• Signs and symptoms of early HIV sero-conversation: fever, rash, oral ulcers, pharyngitis, malaise, fatigue, joint pains, weight loss, myalgia, headache (similar to flu-like symptoms)
• Risk of acquiring Hepatitis B and C from a specific exposure and availability of prophylaxis for this	• Risk of Hepatitis B is 9–30% from a needle stick exposure – the client can be given vaccinations • Risk of Hepatitis is 1–10% after needle stick exposure– there is no vaccinations for this
Note: Provider should correct misconceptions at all times during the counselling sessions	

Psychological support: Many people will feel anxious after exposure. Every exposed person needs to be informed about the risks and the measures that can be taken. This will help to relieve part of the anxiety, but some may require further specialised psychological support.

Documentation on record is essential. **Special leave from work** should be considered for a period of time eg. 2 weeks (initially) then, as required based on assessment of the exposed person's mental state, side effects and requirements.

Practical application in the clinical settings:

- Once prophylactic treatment has begun, the exposed person must sign form A1 (*see annex 11, p 118*).
- Informed consent also means that if the exposed person has been advised PEP, but refuses to start it, s/he should sign Form A1 (*see annex 12, p 120*). This document should be kept by the designated officer for PEP.
- An information sheet covering the PEP and the biological follow-up after any AEB (*see Annex 13, p 121*) may be given to the person under treatment. However, this sheet cannot replace verbal explanations.
- Arrange for follow-up visit and leave from work.

7.4 Step 4: Prescribe PEP

7.4.1 Deciding on PEP regimen

There are two types of regimens:

- Basic regimen: 2-drug combination
- Expanded regimen: 3-drug combination

The decision to initiate the type of regimen depends on the type of exposure and HIV serostatus of the source person. *See Table 53*.

Table 53: HIV Post-exposure Prophylaxis evaluation

Exposure	Status of source		
	HIV+ and asymptomatic	**HIV+ and Clinically symptomatic**	**HIV status unknown**
mild	Consider 2-drug PEP	Start 2- drug PEP	Usually no PEP or consider 2-drug PEP
moderate	Start 2-drug PEP	Start 3-drug PEP	Usually no PEP or consider 2-drug PEP
severe	Start 3-drug PEP	Start 3-drug PEP	Usually no PEP or consider 2-drug PEP

- HIV testing of the source patient should not delay the decision about whether or not to start PEP. Start 2-drugs first if required, then send for consultation or refer.
- In the case of a high risk exposure from a source patient who has been exposed to or is taking antiretroviral medications, consult an expert to choose the PEP regimen, as the risk of drug resistance is high. Refer/consult expert physician. Start 2 drug regimen first.

7.4.2 Expert opinion may be obtained for the following situations

(Refer to list of HIV/PEP experts on www.nacoonline.org)

- Delay in reporting exposure (> 72 hours).
- Unknown source: use of PEP to be decided on case to case basis after considering the severity of exposure and the epidemiologic likelihood of HIV transmission. Do not delay PEP initiation if indicated.
- Known or suspected pregnancy: do not delay PEP if indicated.
- Breastfeeding issues in the exposed person: do not delay PEP if indicated. Consider stopping breast feeding if PEP is indicated.
- Source patient is on ART or possibly has HIV drug resistance : refer/consult as soon as possible.
- Major toxicity of PEP regimen: minor side effects may be managed symptomatically. Refer to expert if non-tolerance or non-adherence.
- Refer/consult if in doubt or complicated cases (eg major psychological problem).

Various animal studies done over the years have provided encouraging evidence of post exposure chemoprophylactic efficacy. Studies have also shown that delaying initiation, shortening the duration or decreasing the antiretroviral dose of PEP, individually or in combination, decreased its prophylactic efficacy. In a retrospective case control study of HCP, it was demonstrated that use of Zidovudine as PEP was associated with a reduction in the risk of HIV infection by approximately 81%. Also the experience in HIV infected patients has shown that combination of different antiretroviral agents is superior to monotherapy regimen, so a combination of two or three drugs in PEP regimen should be more beneficial than a single drug. One needs to consider toxicity of a combination regimen vis-à-vis risk of transmission.

PEP must be initiated as soon as possible, preferably within 2 hours

7.4.3 Initiate HIV chemoprophylaxis

Because post-exposure prophylaxis (PEP) has its greatest effect if begun within 2 hours of exposure, it is essential to act immediately. There is little benefit if >72 hours later. The prophylaxis needs to be continued for 4 weeks.

- Report exposure immediately to appropriate authority.
- Fill in the medical form (*see annex 11*).
- Never delay start of therapy due to debate over regimen. Begin with basic 2-drug regimen, and once expert advice is obtained, change as required.
- The 3rd drug can be added after consultation with an expert.

Table 54: Dosages of the drugs for PEP

Medication	2-drug regimen	3-drug regimen
Zidovudine (AZT)	300 mg twice a day	300 mg twice a day
Stavudine (d4T)	30 mg twice a day	30 mg twice a day
Lamivudine (3TC)	150 mg twice a day	150 mg twice a day
Protease Inhibitors		1st choice : Lopinavir/ritonavir (LPV/r) 400/100 mg twice a day or 800/200 mg once daily with meals 2nd choice : Nelfinavir (NLF) 1250 mg twice a day or 750 mg three times a day with empty stomach 3rd choice : Indinavir (IND) 800 mg every 8 hours and drink 8–10 glasses (≥ 1.5 litres) of water daily

Note: If protease inhibitor is not available and the 3rd drug is indicated, one can consider using Efavirenz (EFV 600 mg once daily). Monitoring should be instituted for side effects of this drug eg CNS toxicity such as nightmares, insomnia etc.

* Fixed Dose Combination (FDC) are preferred, if available. Ritonavir requires refrigeration.

Table 55: PEP regimens to be prescribed by health centers

	Preferred	Alternative
2-drug regimen (basic PEP regimen)	**1st choice:** Zidovudine (AZT) + Lamivudine (3TC)	**2nd choice:** Stavudine (d4T) + Lamivudine (3TC)
3-drug regimen (expanded PEP regimen) - consult expert opinion for starting 3rd drug eg LPV/r, NLF or IND		
Not recommended	ddI + d4T combination NNRTI such as Nevirapine should not be used in PEP	

More information on alternative schedules is available in the latest update USPHS guidelines issued 30 September 2005. (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5409a1.htm) or www.who.int

7.4.4 **Selection of the PEP regimen when the source patient is known to be on ART:** The physician should consider the comparative risk represented by the exposure and information about the exposure source, including history of and response to antiretroviral therapy based on clinical response, CD4 cell counts, viral load measurements (if available), and current disease stage (WHO clinical staging and history). When the source person's virus is known or suspected to be resistant to one or more of the drugs considered for the PEP regimen, the selection of drugs to which the source person's virus is unlikely to be resistant is recommended. Refer for expert opinion.

7.4.5 If this information is not immediately available, **initiation of PEP, if indicated, should not be delayed. Give the 2 drug (basic) regimen.** Changes in the PEP regimen can be made after PEP has been started, as appropriate. Re-evaluation of the exposed person should be considered within 72 hours post-exposure, especially as additional information about the exposure or source person becomes available.

7.4.6 Antiretroviral drugs during pregnancy

If the exposed person is pregnant, the evaluation of risk of infection and need for PEP should be approached as with any other person who has had an HIV exposure. However, the decision to use any antiretroviral drug during pregnancy should involve discussion between the woman and her health-care provider (s) regarding the potential benefits and risks to her and her fetus.

Data regarding the potential effects of antiretroviral drugs on the developing fetus or neonate are limited. There is a clear contraindication for Efavirenz (first 3 months of pregnancy) and Indinavir (pre natal).

In conclusion, for a female HCP considering PEP, a **pregnancy test** is recommended if there is any chance that she may be pregnant. Pregnant HCP are recommended to begin the basic 2-drug regimen, and if a third drug is needed, Nelfinavir is the drug of choice.

7.4.7 Side-effects and adherence to PEP

Studies of HCP taking PEP have reported more side effects than PLHAs taking ART, most commonly nausea and fatigue. Possible side-effects occur mainly at the beginning of the treatment and include nausea, diarrhoea, muscular pain and headache. The person taking the treatment should be informed that these may occur and **should be dissuaded from stopping the treatment** as most side-effects are mild and transient, though possibly uncomfortable. Anaemia and/or leucopenia and/or thrombocytopenia may occur during the month of treatment. A complete blood count and liver function tests (transaminases) may be performed at the beginning of treatment (as baseline) and after 4 weeks.

In practice and from HCP studies, many HCP did not complete the full course of PEP because of side effects. Side effects can be reduced by prescribing regimens that do not include a protease inhibitor (PI), by giving medications to reduce nausea and gastritis and by educating clients about how to reduce side effects eg. taking PEP medications with food. It is important that side effects should be explained before initiating PEP so that the symptoms are not confused with symptoms of seroconversion to HIV.

Adherence information is essential with psychological support. More than 95% adherence is important in order to maximise the efficacy of the medication in PEP.

Table 56: Management of Minor ARV drug side effects	
Signs or symptoms	**Management at health facility**
Nausea	Take with food. If on AZT, reassure that this is common, usually self-limited. Treat symptomatically
Headache	Give paracetamol. Assess for meningitis. If on AZT or EFV, reassure that this is common and usually self-limited. If persists more than 2 weeks, call for advice or refer
Diarrhoea	Hydrate. Follow diarrhoea guidelines. Reassure patient that if due to ARV, this will improve in a few weeks. Follow up in 2 weeks. If not improved, call for advice or refer
Fatigue	This commonly lasts 4 to 6 weeks especially when starting AZT. Give 'sick leave' from work. If severe or longer than this, call for advice or refer
CNS side effects: Anxiety, nightmares, psychosis, depression	This may be due to EFV. Take EFV at night before sleeping; counsel and support (usually lasts < 3 weeks). Initial difficult time can be managed with amitriptyline at bedtime Call for advice or refer if severe depression or suicidal tendencies or psychosis (stop EFV)
Blue /black nails	Reassure. It is a non-threatening side effect, common with AZT
Rash	If on EFV, assess carefully. Is it a dry or wet lesion? Call for advice. If generalised or peeling, stop drugs and refer for expert opinion
Fever	Assess clinically for hepatitis or if this could be primary (acute) HIV infection or other non-HIV related infections eg concurrent common cold. Call for advice or refer
Jaundice or abdominal or flank pain	Stop drugs. Call for advice or refer (Abdominal pain may be pancreatitis from d4T.) If jaundice or liver tenderness, send for ALT test and stop ARVs. Call for advice or refer
Pallor	Measure Haemoglobin. Refer if sever pallor or symptoms of anaemia or very low haemoglobin (<8 grams). This may be due to AZT
Tingling, numbers or painful feet/legs	If new or worse on treatment, call for advice or refer. Patient on d4T/3TC should have the d4T discontinued – substitute AZT if no anaemia (check haemoglobin)

7.4.8 Amount of medication to dispense for PEP

All clients starting on PEP must take 4 weeks (28 days) of medication. In all cases, the **first dose of PEP** should be offered as soon as possible, once the decision to give PEP is made. HIV testing or results of the source HIV test can come later. As usage of PEP drugs is not frequent and the shelf life is 1 to 1.5 years, it is proposed that **starter packs for 7 days** can be put in the emergency department with instructions to go to a designated clinic/officer within 1–3 days for a complete risk assessment, HIV counselling and testing and dispensing of the rest of the medications and management. At least 3 such kits are provided in the casualty department.

It is important to monitor and regularly follow-up the person once PEP is started (*see step 6, p 87*).

7.4.9. Hepatitis B

All health staff should be vaccinated against hepatitis B. The vaccination for Hepatitis B consists of 3 doses: initial, 1 month, and 6 months. Sero-conversion after completing the full course is 99%.

If the exposed person is unvaccinated or unclear vaccination status give complete hepatitis B vaccine series.

Table 57: HBV vaccination after an AEB

HBV vaccination status of exposed person	Action after AEB
Never vaccinated	Give complete hepatitis B vaccine series
Vaccinated, anti-HB-S not known	Give Hep B Vaccine Booster
Vaccinated more than 5 years ago	Give Hep B Vaccine Booster

Note: If available, testing for the antibody level (anti-HbS) is not necessary.
Hep B vaccine should be given as soon as possible after exposure.
Do not wait for anti-HbS results, if test is done.
Adequate levels of serum Ab to HbSAg (i.e anti-HbS) is $\geq$ 10 IU/L

7.4.10 Hepatitis C

There is presently no prophylaxis available against hepatitis C. There is no evidence that interferon, pegalated or not, with or without ribavirin is more effective when given at this time than when given at the time of disease. Post-exposure management for HCV is based on early identification of chronic HCV disease and referral to a specialist for management.

7.5 Step 5: Laboratory Evaluation

The reason for HIV testing soon after an occupational exposure is to establish a "baseline" against which to compare future test results. If the HCP is HIV-negative at the baseline test, it is in principle possible to prove that subsequent infection identified by follow-up testing is related to the occupational exposure (depending on the timing of infection and consideration of other risks or exposures). When offered HIV testing, the exposed person should receive standard pre-test counselling according to the national HIV testing and counselling guidelines, and should give informed consent for testing. Confidentiality of the test result must be ensured.

There are different reasons for possibly delaying HIV testing: the HCP may be unable to give informed consent immediately after the exposure due to anxiety, the exposure occurs outside working hours or in settings where HIV testing is not readily available. The HIV test may be done up to several days after the exposure, based on informed consent and with pre- and post-test counselling and ensuring confidentiality.

Do not delay PEP if HIV testing is not available.

Table 58: Recommended baseline laboratory evaluation

Timing	In persons taking PEP (standard regimen)	In persons not taking PEP
Baseline (within 8 days after AEB)	HIV, HCV, anti-HBs* Complete blood count Transaminases	HIV, HCV, anti-HBs *

* *HIV, HBV and HCV testing of exposed staff within 8 days of an AEB is required (baseline serostatus).* ***Offer an HIV test in case of an AEB, as a positive HIV status may indicate the need to discontinue PEP****. The decision on whether to test for HIV or not should be based on informed consent of the exposed person.*

HIV RNA testing by polymerase chain reaction (PCR) during PEP has a very poor positive predictive value and should be strongly discouraged.

Pregnancy testing should also be available, but its unavailability should not prevent the provision of PEP.

Other laboratory testing such as haemoglobin estimation should be available, especially when AZT is used for PEP in areas where anaemia is common.

Testing for other blood-borne diseases such as syphilis, malaria and kala-azar may also be useful, depending on the nature of risk, symptoms of the source patient, local prevalence and laboratory capacity.

7.6 Step 6: Follow-up of an Exposed Person

Whether or not PEP prophylaxis has been started, follow up is indicated to monitor for possible infections and provide psychological support.

7.6.1 Clinical follow-up

In addition, in the weeks following an AEB, the exposed person must be monitored for the eventual appearance of signs indicating an HIV seroconversion: acute fever, generalised lymphadenopathy, cutaneous eruption, pharyngitis, non-specific flu symptoms and ulcers of the mouth or genital area. These symptoms appear in 50%-70% of individuals with an HIV primary (acute) infection and almost always within 3 to 6 weeks after exposure. When a primary (acute) infection is suspected, referral to an ART centre or for expert opinion should be arranged rapidly.

An exposed person should be advised to use precautions (e.g., avoid blood or tissue donations, breastfeeding, unprotected sexual relations or pregnancy) to prevent secondary transmission, especially during the first 6–12 weeks following exposure. **Condom use is essential**.

Adherence and side effect counseling should be provided and reinforced at every follow-up visit. Psychological support and mental health counseling is often required.

7.6.2 Laboratory follow-up

Follow-up HIV testing: exposed persons should have post-PEP HIV tests. Testing at the completion of PEP may give an initial indication of seroconversion outcome if the available antibody test is very sensitive. However, testing at 4–6 weeks may not be enough as *use of PEP may prolong the time to seroconversion;* and there is not enough time to diagnose all persons who seroconvert. Therefore, **testing at 3 months and again at 6 months is recommended.** Very few cases of seroconversion after 6 months has been reported. Hence, no further testing is recommended if the HIV test at 6 months is negative.

Table 59: Recommended follow-up laboratory tests

Timing	In persons taking PEP (standard regimen)	In persons not taking PEP
Weeks 2 and 4	Transaminases* Complete blood count §	Clinical monitoring for hepatitis
Week 6	HIV-Ab	HIV-Ab
Month 3	HIV-Ab, anti-HCV, HBsAg Transaminases*	HIV-Ab, anti-HCV, HBsAg
Month 6	HIV-Ab, anti-HCV, HBsAg Transaminases*	HIV-Ab, anti-HCV, HBsAg

* *Transaminases should be checked at week 2 and 4 to detect hepatitis in case the exposed person contracted HBV from the AEB.*

§ *For persons started on AZT-containing PEP regimens*

B8 Section

Implementation of PEP in the Healthcare Facility: Operationalizing the PEP Programme to Ensure Access to PEP Drugs Round-the-clock

8.1 Responsibility of the Medical Superintendent of the Hospital

As with all other functions of a healthcare facility, the ultimate responsibility for prevention and control of infection rests with the hospital administrator. The Medical Superintendent (MS)/Dean/Principal/In-charge of the Hospital must consitute a hospital **infection control committee** which will oversee and monitor hospital infection control including universal precaution and post-exposure prophylaxis implementation.

The MS must ensure that the hospital has a written protocol to handle occupational exposure and that these are disseminated to all relevant personnel/departments and displayed at convenient/prominent locations within the hospital, for the information of staff. The Medical Superintendent of the hospital has the responsibility of informing all staff about:

- the universal precautions to be followed in health services
- use of personal protective equipment
- other preventive measures to be taken against these viruses (including vaccination) especially Hep B vaccine
- procedures to be followed in case of accidental exposure to blood and body fluids

Each institution should designate a team of persons who has the authority to ensure that confidentiality of the HCP is maintained and the required care is given in any case of occupational exposure.

8.2 Role of the Infection Control Committee and Infection Control Core Group

The infection control committee is established by the hospital administration and provides a forum for multidisciplinary input and cooperation, and information sharing. This committee should include the following representation from relevant departments: administration, medicine, other clinical departments, nursing staff, clinical microbiology, pharmacy, waste management/housekeeping services. The committee will report to the administration directly.

The infection control committee is responsible for the development of policies for the prevention and control of infection and to oversee the implementation of the infection control program. This includes:

- Electing one member of the committee as chairperson (who will have direct access to the head of the hospital administration)
- Appoint an infection control practitioner as secretary (Health care provider trained in principles and practices of infection control eg physician, microbiologist or infection control nurse)
- Meet regularly – ideally monthly but minimum three times a year
- Develop for the hospital, the infection control manual/standard operating procedures, injury register etc.

- Monitor and evaluate the performance of the infection control programme
- Appoint an infection control core group
- Ensure that the Monthly Hospital PEP reporting form be sent to SACS/NACO monthly (*see annex 14, p 122*).

Infection control core group/working group: is responsible for the day-to-day activities of the infection control programme. They will have a direct reporting responsibility to the hospital administration.

The infection control team will:

- Assess training needs of the staff and provide required training through the awareness program, in-service education and on-the job training
- Organise regular training programme for the staff for essential infection control practices appropriate for their nature of work
- Provide periodic re-training or orientation of staff and review the impact of training
- Review and monitor practices of infection control in the healthcare facility with feedback to the hospital infection committee and hospital administration

8.3 Access and Availability to PEP at the Healthcare Facility

In order to ensure that an exposed person has access to prophylactic therapy in a timely manner, it is recommended that PEP drugs be kept available round-the-clock in any **one** location where a doctor is on-call 24-hours a day (e.g. casualty, ICU). All health staff should know through in-house trainings where to get PEP as required.

Table 59: Drug stock at the healthcare facility

Level of health care facility	Designated person/team in charge of PEP	Minimum drug stock of PEP exposure-response kits*
Tertiary hospitals and medical colleges	**Team:** Infection control officer, Physician, Casualty officer Where ART centers are within the same institution, the ART nodal officer should be the reference person for PEP	3 kits of 7 days supply ie. FDC (AZT/3TC) 2 tabs/day x 7 days x 3 kits = 42 tabs If ART centre available, to link for supply and referrals
Secondary –district, taluk	**Team:** infection control officer, casualty officer The district/taluk physician (internal medicine) should be the reference person for PEP	3 kits of 5 days supply Ie. FDC (AZT/3TC) 2 tabs/day x 5 days x 3 kits = 30 tabs If ART centre available, to link for supply and referrals
Primary – CHC	The medical officer of the CHC is the reference person for PEP	2 kits of 3 days supply. Ie FDC (AZT/3TC) 2 tabs/day x 3 days x 2 kits = 12 tabs
Primary Health centers (PHC)	The PHC medical officer is in-charge of referring for PEP to CHC or district level	Link to CHC or district level for PEP

* PEP kit comprises of the 2 drug regimen: AZT (300mg) + 3TC (150mg) as a fixed dose combination

For the full course of drugs, this can be purchased locally to complete 4 weeks of drugs or refer to nearest ART centre. In case these drugs are not available on site at the healthcare facility, the hospital can purchase it locally and it shall be **reimbursed by SACS.**

The following are the **minimum provisions of PEP** in health care facilities:

- A minimum of 72 hours worth of 2 drugs in the basic regimen should be included in the HIV exposure-response kit
- Reporting/written consent forms **(annex 11, 12, 14)**
- Information sheet for the exposed person **(annex 13)**
- Maintain confidentiality
- Rapid HIV test kit to be used to test the source patient/exposed person should be available in the hospital or if not, referral to next level (eg from PHC to district hospital) should be possible.
- List of referral persons and nearest laboratory testing sites for HIV, HBV,HCV
- The names and contact details of at least 3 trained doctors for PEP should be displayed in the casualty of the hospital.

District hospitals with PEP services should have extra stock to replenish the used kits. Ideally they also manage the expiry dates for example, if the PEP kit reaches 3 months prior to expiry, it should be exchanged so that the expiring ARVs can be used in time. If there is an ART centre available, it is recommended to link up with the ART centre to ensure referral and exchange linkages.

Because of the complexity of selection of HIV PEP regimens, consultation with a HIV physician is strongly recommended. This can be especially important in management of a pregnant or breastfeeding worker or a worker who has been exposed to a heavily HIV treatment-experienced source.

Section

ANNEXES

1 Annex

Presumptive and Definitive Criteria for Recognising HIV-Related Clinical Events in Adults and Adolescents

Clinical event	Clinical diagnosis	Definitive diagnosis
Clinical Stage 1		
Asymptomatic	No HIV related symptoms reported and no signs on examination	Not applicable
Persistent generalized lymphadenopathy (PGL)	Painless enlarged lymph nodes >1 cm, in two or more non-contiguous sites (excluding inguinal), in absence of known cause and persisting for 3 months	Histology
Clinical Stage 2		
Moderate unexplained weight loss (<10% of body weight)	Reported unexplained weight loss. In pregnancy failure to gain weight	Documented weight loss <10% of body weight
Recurrent bacterial upper respiratory tract infections (current event plus one or more in last six-month period)	Symptom complex, e.g. unilateral face pain with nasal discharge (sinusitis), painful inflamed eardrum (otitis media), or tonsillo-pharyngitis without features of viral infection (e.g. coryza, cough)	Laboratory studies where available, e.g. culture of suitable body fluid
Herpes zoster	Painful vesicular rash in dermatomal distribution of a nerve supply does not cross midline	Clinical diagnosis
Angular chelitis	Splits or cracks at the angle of the mouth not due to iron or vitamin deficiency, and usually respond to antifungal treatment	Clinical diagnosis
Recurrent oral ulcerations (two or more episodes in last six months)	Aphthous ulceration, typically painful with a halo of inflammation and a yellow-grey pseudomembrane	Clinical diagnosis
Papular pruritic eruption	Papular pruritic lesions, often with marked post-inflammatory pigmentation	Clinical diagnosis
Seborrhoeic dermatitis	Itchy scaly skin condition, particularly affecting hairy areas (scalp, axillae, upper trunk and groin)	Clinical diagnosis
Fungal nail infections	Paronychia (painful red and swollen nail bed) or onycholysis (separation of the nail from the nail bed) of the fingernails (white discolouration—especially involving proximal part of nail plate – with thickening and separation of nail from nail bed)	Fungal culture of nail/nail plate material

Clinical event	Clinical diagnosis	Definitive diagnosis
Clinical Stage 3		
Severe unexplained weight loss (more than 10% of body weight)	Reported unexplained weight loss (>10% of body weight or body mass index <18.5). In pregnancy weight loss may be masked	Documented loss of more than 10% of body weight
Unexplained chronic diarrhoea for longer than one month	Chronic diarrhoea (loose or watery stools three or more times daily) reported for longer than one month	Not required but confirmed if three or more stools observed and documented as unformed, and two or more stool tests reveal no pathogens
Unexplained persistent fever (intermittent or constant and lasting for longer than one month)	Reports of fever or night sweats for more than one month, either intermittent or constant with reported lack of response to antibiotics or antimalarials, without other obvious foci of disease reported or found on examination. Malaria must be excluded in malarial areas	Documented fever >37.6. with negative blood culture, negative Ziehl-Nielsen (ZN) stain, negative malaria slide, normal or unchanged chest X-ray (CXR) and no other obvious focus of infection
Oral candidiasis	Persistent or recurring creamy white curd-like plaques which can be scraped off (pseudomembranous), or red patches on tongue, palate or lining of mouth, usually painful or tender (erythematous form)	Clinical diagnosis
Oral hairy leukoplakia	Fine white small linear or corrugated lesions on lateral borders of the tongue, which do not scrape off	Clinical diagnosis
Pulmonary TB (current)	Chronic symptoms: (lasting 2–3 weeks) cough, haemoptysis, shortness of breath, chest pain, weight loss, fever, night sweats, PLUS either positive sputum smear OR Negative sputum smear AND compatible chest radiograph (including but not restricted to upper lobe infiltrates, cavitation, pulmonary fibrosis and shrinkage). No evidence of extrapulmonary disease	Isolation of *M. tuberculosis* on sputum culture or histology of lung biopsy (together with compatible symptoms)
Severe bacterial infection (e.g. pneumonia, meningitis, empyema, pyomyositis, bone or joint infection, bacteraemia, severe pelvic inflammatory disease)	Fever accompanied by specific symptoms or signs that localize infection, and response to appropriate antibiotic	Isolation of bacteria from appropriate clinical specimens (i.e. usually sterile sites)
Acute necrotizing ulcerative gingivitis or necrotizing ulcerative periodontitis	Severe pain, ulcerated gingival papillae, loosening of teeth, spontaneous bleeding, bad odour, and rapid loss of bone and/or soft tissue	Clinical diagnosis
Clinical Stage 4		
HIV wasting syndrome	Reported unexplained weight loss (>10% body weight), with obvious wasting or body mass index <18.5 PLUS EITHER unexplained chronic diarrhoea (loose or	Documented weight loss >10% of body weight; plus two or more unformed stools negative for pathogens

Clinical event	Clinical diagnosis	Definitive diagnosis
Clinical Stage 4		
	watery stools three or more times daily) reported for longer than one month. or Reports of fever or night sweats for more than one month without other cause and lack of response to antibiotics or antimalarials. Malaria must be excluded in malarial areas	or Documented temperature of > 37.6 °C or more with no other cause of disease, negative blood culture, negative malaria slide and normal or unchanged CXR
Pneumocystis pneumonia	Dyspnoea on exertion or nonproductive cough of recent onset (within the past 3 months), tachypnoea and fever; AND Chest x-ray evidence of diffuse bilateral interstitial infiltrates AND No evidence of a bacterial pneumonia. Bilateral crepitations on auscultation with or without reduced air entry	Cytology or immunofluorescent microscopy of induced sputum or bronchoalveolar lavage (BAL), or histology of lung tissue
Recurrent bacterial pneumonia (this episode plus one or more episodes in last 6 months)	Current episode plus one or more previous episodes in last 6 months. Acute onset (<2 weeks) of symptoms (e.g. fever, cough, dyspnoea, and chest pain) PLUS new consolidation on clinical examination or CXR. Response to antibiotics	Positive culture or antigen test of a compatible organism
Chronic herpes simplex virus (HSV) infection (orolabial, genital or anorectal) of more than one month duration	Painful, progressive anogenital or orolabial ulceration; lesions caused by recurrent HSV infection and reported for more than one month. History of previous episodes. Visceral HSV requires definitive diagnosis	Positive culture or DNA (by PCR) of HSV or compatible cytology/histology
Oesophageal candidiasis	Recent onset of retrosternal pain or difficulty on swallowing (food and fluids) together with oral candidiasis	Macroscopic appearance at endoscopy or bronchoscopy, or by microscopy/ histology
Extrapulmonary TB	Systemic illness (e.g. fever, night sweats, weakness and weight loss). Other evidence for extrapulmonary or disseminated TB varies by site: Pleural, pericardial, peritoneal involvement, meningitis, mediastinal or abdominal lymphadenopathy, osteitis. Miliary TB diffuse uniformly distributed small miliary shadows or micronodules on CXR Discrete cervical lymph node *M. tuberculosis* infection is usually considered a less severe form of extra pulmonary tuberculosis	*M. tuberculosis* isolation or compatible histology from appropriate site, together with compatible symptoms/ signs (if culture/histology is from respiratory specimen then must other have evidence of extra pulmonary disease)
Kaposi's sarcoma	Typical appearance in skin or oropharynx of persistent, initially flat, patches with a pink or blood-bruise colour, skin lesions that usually develop into violaceous plaques or nodules	Macroscopic appearance at endoscopy or bronchoscopy, or by histology
CNS toxoplasmosis	Recent onset of a focal neurological abnormality or reduced level of consciousness AND response within 10 days to specific therapy	Positive serum toxoplasma antibody AND (if available) single/multiple intracranial mass lesion on neuro-imaging

Clinical event	Clinical diagnosis	Definitive diagnosis
Clinical Stage 4		
HIV encephalopathy	Clinical finding of disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing over weeks or months in the absence of a concurrent illness or condition other than HIV infection which might explain the findings	Diagnosis of exclusion: and (if available) neuro-imaging (CT or MRI)
Extrapulmonary cryptococcosis (including meningitis)	Meningitis: usually sub acute, fever with increasing severe headache, meningism, confusion, behavioural changes that responds to cryptococcal therapy	Isolation of *Cryptococcus neoformans* from extrapulmonary site or positive cryptococcal antigen test (CRAG) on CSF/blood
Disseminated non-tuberculous mycobacteria infection	No presumptive clinical diagnosis	Diagnosed by finding atypical mycobacterial species from stool, blood, body fluid or other body tissue, excluding lung
Progressive multi focal leukoencephalopathy (PML) PML	No presumptive clinical diagnosis	Progressive neurological disorder (cognitive dysfunction, gait/speech disorder, visual loss, limb weakness and cranial nerve palsies) together with hypodense white matter lesions on neuro-imaging or positive polyomavirus (JCV) PCR on CSF
Cryptosporidiosis (with diarrhoea lasting more than one month)	No presumptive clinical diagnosis	Cysts identified on modified ZN microscopic examination of unformed stool
Chronic isosporiasis	No presumptive clinical diagnosis	Identification of *Isospora*
Disseminated mycosis (coccidiomycosis, histoplasmosis)	No presumptive clinical diagnosis	Histology, antigen detection or culture from clinical specimen or blood culture
Recurrent non-typhoid salmonella bacteraemia	No presumptive clinical diagnosis	Blood culture
Lymphoma (cerebral or B cell non-Hodgkin) or other solid HIV associated tumours	No presumptive clinical diagnosis	Histology of relevant specimen or for CNS tumours neuroimaging techniques
Invasive cervical carcinoma	No presumptive clinical diagnosis	Histology or cytology
Visceral leishmaniasis	No presumptive clinical diagnosis	Diagnosed by histology (amastigotes visualized) or culture from any appropriate clinical specimen
HIV-associated nephropathy	No presumptive clinical diagnosis	Renal biopsy
HIV-associated cardiomyopathy	No presumptive clinical diagnosis	Cardiomegaly and evidence of poor left ventricular function confirmed by echocardiography

Source: Revised WHO Clinical Staging and Immunological Classification of HIV and case definition of HIV for surveillance, May 2006

2 Annex

ARV Drug Combinations and Strategies not to be used

Some antiretroviral regimens or components are not recommended for HIV-1 infected patients due to sub-optimal antiviral potency, unacceptable toxicity, or pharmacological concerns. These are summarized below:

ARV drug combinations not to use:

ARV combinations	Reason not to use
Monotherapy or dual therapy to treat chronic HIV infection	Rapid development of resistance
d4T + AZT	Antagonism (reduced levels of both drugs)
d4T + ddI	Overlapping toxicities (pancreatitis, hepatitis, lipoatrophy, peripheral neuropathy, lactic acidosis) Deaths reported in pregnant women
3TC + FTC	Interchangeable, but should not be used together
TDF + 3TC + ABC **or** TDF + 3TC + ddI	Select for K65R mutation and are associated with high incidence of early virological failure
TDF + ddI + any NNRTI	High incidence of early virological failure
Unboosted PIs	Poor bioavailability and higher pill burden.

Antiretroviral strategies not recommended

1. Induction-maintenance: Initiation of three drug ART and then reducing it to a combination of two ARV drugs is not recommended.
2. Sequential adding of drugs: A third drug, especially NNRTI should not be added to an on-going two drug regimen, as it can lead to rapid selection of resistance.
3. Structured treatment interruptions: Any form of treatment interruptions is not recommended in clinical practice.

3 Annex

Dosages of Antiretroviral Drugs for Adults and Adolescents

Generic name	Dose	
Nucleoside RTIs		
Abacavir (ABC)	300 mg twice daily or 600 mg once daily	
Zidovudine (AZT)	300 mg twice daily	
Emtricitabine (FTC)	200 mg once daily	
Didanosine (ddI)[1] buffered tabs or enteric coated (EC) caps	>60 kg: 400 mg once daily <60 kg: 250 mg once daily	
Lamivudine (3TC)	150 mg twice daily or 300 mg once daily	
Stavudine (d4T)	30 mg twice daily	
Nucleotide RTIs		
Tenofovir	300 mg once daily	
Non-nucleoside RTIs		
Efavirenz (EFV)	600 mg once daily	
Nevirapine (NVP)	200 mg once daily for 14 days (lead-in dose); followed by 200 mg twice daily	
Proteases inhibitors		
Atazanavir/ritonavir (ATV/r)	300 mg/100 mg once daily	
Fos-amprenavir/ritonavir (FPV/r)	700mg/100 mg twice daily	
Indinavir/ritonavir (IDV/r)	800 mg/100 mg twice daily	
Lopinavir/ritonavir (LPV/r)[2]	Capsule Lopinavir 133 mg + ritonavir 33 mg	Three capsules twice daily (ie 400/100mg twice daily) Four capsules twice daily when combined with EFV or NVP (533/133 mg twice daily)
	Tablet (heat stable formulation) Lopinavir 200mg + ritonavir 50mg	Treatment naïve patients Two tablets twice daily irrespective of co-administration with EFV or NVP (400/100 mg twice daily)
		Treatment experienced patients Three tablets twice daily when combined with EFV or NVP (600/150 mg twice daily)
Nelfinavir (NFV)	1250 mg twice daily	
Saquinavir/ ritonavir (SQV/r)	1000/100 mg twice daily	

1 ddI dose should be adjusted when co-administered with tenofovir. If weight >60 kg, give ddI at 250 mg once daily. If weight <60 kg, give ddI at 200 mg once daily.

2 See TB section for TB-specific dose modifications of lopinavir/r .

4 Annex

Clinical signs and Symptoms and Management of Adverse Effects of Antiretroviral Drugs

Adverse effect	Possible offending drug(s)	Clinical signs/symptoms	Management
Acute hepatitis	Nevirapine (NVP) and PI/r; Efavirenz (EFZ) less common; Uncommon with zidovudine (AZT), didanosine (ddI), stavudine (d4T) (<1%);	Jaundice, liver enlargement, gastrointestinal symptoms, fatigue, anorexia NVP-associated hepatitis may have hypersensitivity component (drug rash, systemic symptoms, eosinophilia)	If possible, monitor serum transaminases and bilirubin. If ALT > 5 times the baseline level, stop ARVs until symptoms resolve. NVP should be permanently discontinued. Substitute the most likely offending ARV drug
Acute pancreatitis	ddI, d4T Lamivudine (3TC) (infrequent)	Nausea, vomiting and abdominal pain	If possible, monitor serum pancreatic amylase, lipase. All ART should be stopped until symptoms resolve. Restart ART with change to different NRTI, preferably one without pancreatic toxicity (e.g. AZT, TDF, ABC)
Lactic acidosis	All nucleoside analogue reverse transcriptase inhibitors (NRTIs) particularly D4T and ddI	Initial symptoms are variable: a clinical prodromal syndrome may include generalized fatigue and weakness, gastrointestinal symptoms (nausea, vomiting, diarrhoea, abdominal pain, hepatomegaly, anorexia, and/or sudden unexplained weight loss), respiratory symptoms (tachypnoea and dyspnoea) or neurological symptoms (including motor weakness)	Discontinue all ART; symptoms may continue or worsen after discontinuation of ART. Give supportive therapy. Resume ART with replacing the offending NRTI with either ABC, TDF
Hyper-sensitivity reaction	Abacavir (ABC) Nevirapine (NVP)	ABC: Constellation of acute onset of symptoms including: fever, fatigue, myalgia, nausea/vomiting, diarrhoea, abdominal pain, pharyngitis, cough, dyspnoea (with or without rash). While these symptoms overlap those of common infectious illnesses,	Discontinue all ART until symptoms resolve. The reaction progressively worsens with drug administration and can be fatal. Administer supportive therapy. Do not rechallenge with ABC (or NVP), as anaphylactic reactions and death have been reported. Once symptoms resolve, restart

Adverse effect	Possible offending drug(s)	Clinical signs/symptoms	Management
		the combination of acute onset of both respiratory and gastrointestinal symptoms after starting ABC is more typical of a hypersensitivity reaction **NVP:** Systemic symptoms of fever, myalgia, arthralgia, hepatitis, eosinophilia with or without rash	ART with a change to different NRTI if ABC-associated or to PI- or NRTI -based regimen if NVP-associated
Rash/drug eruptions-including Stevens-Johnson syndrome or toxic epidermal necrolysis (TEN)	Nevirapine (NVP), Efavirenz (EFV-rarely)	Rash usually occurs during the first two to four weeks of treatment. The rash is usually erythematous, maculopapular, confluent, most prominent on the body and arms, may be pruritic and can occur with or without fever. Life-threatening Stevens-Johnson syndrome or toxic epidermal necrolysis has been reported in ~0.3% of infected individuals receiving NVP	In mild cases, give anti-histamines. If rash is moderate, non-progressing and without mucosal or systemic symptoms, consider substituting NVP to EFV after rash resolves. In moderate and severe cases, discontinue all ARVs until symptoms resolve and give supportive treatment. Permanently discontinue NVP for rash with systemic symptoms such as fever, severe rash with mucosal lesions or urticaria, or Stevens-Johnson syndrome or toxic epidermal necrolysis. Once resolved, switch ART regimen to different ARV class (e.g. three NRTIs or two NRTIs and PI)
Peripheral neuropathy	ddI, d4T, 3TC	Pain, tingling, numbness of hands or feet; distal sensory loss, mild muscle weakness, and areflexia can occur	Stop suspect NRTI early and switch to different NRTI that does not have neurotoxicity (e.g. AZT, ABC). Symptoms usually resolve in two to three weeks
Diarrhoea	ddI, NLF, LPV/r, SQV/r	Loose or watery diarrhoea	Usually self-limited. No need to discontinue ART. Offer symptomatic treatment
Dyslipidaemia, Insulin resistance and hyperglycaemia	PIs EFV		Consider replacing the suspected PI by drugs with less risk of metabolic toxicity
GI intolerance	All ARVs	Gastritis, indigestion etc	Usually self-limited. No need to discontinue ARVs. Offer symptomatic treatment
Haematological toxicities eg anaemia and leucopenia	AZT	Fatigue, breathlessness, palpitation	If severe (Hb < 6.5 g/dl and/or absolute nuetrophil count < 500 cells/mm3) – substitute with an NNRTI which has less effect on bone marrow eg D4T, ABC or TDF. Consider blood transfusion

Adverse effect	Possible offending drug(s)	Clinical signs/symptoms	Management
Lipoatrophy and Lipodystrophy	All NRTIs (particularly d4T)	Lipodystrophy syndrome: Dyslipidemia consisting of elevated total cholesterol, low high-density lipoprotein (HDL) cholesterol and elevated triglycerides; Insulin resistance with hyperglycemia; Central fat accumulation (visceral, breast, neck) and local fat accumulation (lipomas, "buffalo hump"); Generalized diminution of subcutaneous fat mass (lipoatrophy). Lipoatrophy includes loss of subcutaneous fat in the face, extremities and buttocks	Early replacement of the suspected ARV drugs (eg D4T) with TDF or ABC. Consider aesthetic treatment and physical exercises
Neuropsychiatric changes	EFV	High rates of CNS effects in the first 2–3 weeks eg confusion, abnormal thinking, nightmares, impaired concentration, depersonalization, abnormal dreams, dizziness, insomnia, euphoria, hallucinations. Severe depression has been reported in 2.4%	Usually self-limited. No need to discontinue unless severe psychosis Counsel to take EFV at night before bedtime
Renal Toxicity (nephrolithiasis)	Indinavir (IND)	Acute flank pain, may have systemic signs eg fever	Stop IND and hydrate, monitor renal functions and symptomatic treatemtn. Consider substituting with another PI
Renal Toxicity (renal tubular dysfunction)	TDF	Features of Fanconi syndrome ie. Hypophosphataemia, hypouricaemia, proteinuria, normoglycaemic glycosuria. Acute renal failure has been reported. Risk factors—low body weight and pre-existing renal disease	Discontinue TDF and give supportive treatment. After resolution, replace with another ARV

Note: Discontinuing the offending agent would mean substituting with an alternative drug to ensure efficacy of HAART regimen.

5 Annex

Drug Interactions with ARVs

ARV	NVP	EFV	LPV/r	NFV	SQV
Anti-Tuberculous drugs					
Rifampicin	πNVP level by 20–58%. Virological consequences are uncertain; the potential of additive hepatotoxicity exists. Co-administration is recommended only be done with careful monitoring	πEFV level by 25% Standard dosing of EFV recommended	πLPV AUC by 75% Should not co-administer	πNFV level by 82% Should not co-administer	πSQV level by 84% Severe liver impairment with co-administer reported Should not co-administer
Rifabutin	Levels: NVPπ16%. No dose adjustment.*	Levels: EFV unchanged; Rifabutin π35% Dose: νrifabutin dose to 450–600 mg Once daily or 600 mg 3x/ week. EFV: Standard	Levels: Rifabutin AUCν3-fold. 25 Decrease rifabutin dose to 150 mg once daily or 3x/week LPV/r: Standard	Levels: NFV π 82%. Should not be co-administered.	Levels: SQVπ40%. Contraindicated unless SQV/RTV. Dose: Rifabutin 150 mg once daily or 3x/week
Clarithromycin	None	πClarithromycin by 39% Monitor for efficacy or use alternative drugs	νClarithromycin AUC by 75%, adjust clarithromycin dose if renal impairment	No data	Without RTV, νclarithromycin level by 45%, νSQV level 177% RTV can νClarithromycin level by 75% No clarithromycin dose adjustment needed for unboosted SQV. For boosted SQV if renal impairment – no data

ARV	NVP	EFV	LPV/r	NFV	SQV
Antifungal					
Ketoconazole	↓Ketoconazole level by 63% ↓NVP level by 15–30% Do not recommend co-administer	No significant changes in ketoconazole or EFV levels	↓LPV AUC ↓Ketoconazole level 3-fold Do not exceed 200mg/day ketoconazole	No dose adjustment necessary	↓SQV level by 3 fold No dose adjustment necessary if given unboosted. For RTV-boosted SQV – no data (RTV treatment dose can increase ketoconazole level 3-fold)
Fluconazole	↓NVP Cmax, AUC, Cmin by 100% No change in fluconazole level Possible increase hepatotoxicity with co-administer requiring monitoring of NVP toxicity	No data	No data	No data	No data
Itraconazole	No data	No data	↓Itraconazole level Do not exceed 200mg/day itraconazole	No data but potential for bidirectional inhibition, monitor toxicities	Bidirectional interaction has been observed. May need to decrease itraconazole dose. Consider monitor SQV level (especially if given unboosted with RTV)
Oral contraceptives					
Ethinyl oestradiol	↑Ethinyl oestradiol by 20%. Use alternative or additional methods	↑Ethinyl oestradiol by 37%. Use alternative or additional methods	↑Ethinyl oestradiol level by 42% Use alternative or additional methods	↑levels of norethindrone by 18% and ethinyl oestradiol by 47%	No data for unboosted SQV. RTV treatment dose can level of ethinyl oestradiol by 41%
Anticonvulsants					
Carbamazepine Phenytoin	Use with caution. One case report showed low EFV concentrations with phenytoin.	Unknown. Use with caution	Many possible interactions: Carbamazepine ↓levels when co-administered with RTV. Use with caution	Unknown, but may decrease NFV levels substantially. Monitor anticonvulsant levels and	Unknown, but may markedly ↑SQV levels. Monitor anticonvulsant levels and consider

ARV	NVP	EFV	LPV/r	NFV	SQV
			Monitor anticonvulsant levels. Phenytoin: π levels of LPV, RTV, andπ levels of phenytoin when administered together. Avoid concomitant use or monitor LPV level.	virological response.	obtaining SQV level.
Opiod Substitution Treatment (OST)					
Methadone	Levels: NVP unchanged. methadoneπ significantly. Opiate withdrawal common when this combination is used. Increased methadone dose often necessary. Titrate methadone dose to effect.	Levels: methadoneπ 60%. Opiate withdrawal common, increase methadone dose often necessary. Titrate methadone dose to effect.	Methadone AUC π 53%. Opiate withdrawal may occur. Monitor and titrate dose if needed. May requireν methadone dose.	NFV may decrease methadone levels, but opiate withdrawal rarely occurs. Monitor and titrate dose if needed. May require methadone dose.	Methadone AUC π 20%. When co-administered with SQV/RTV 400/400 mg BID. No adjustment for this PI regimen, but monitor and titrate to methadone response as necessary.
Buprenorphine	Not studied	Buprenorphine levels π50% nut no withdrawals reported. No dose adjustment is recommended	No significant interactions	No significant interactions	No significant interactions
Lipid lowering agents					
Simvastatin, Lovastatin	No data	πSimvastatin level by 58% EFV level unchanged Adjust simvastatin dose according to lipid response, not to exceed the maximum recommended dose	Potential large νstatin level Avoid concomitant use	νSimvastatin AUC by 505% Potential largeν lovastatin AUC Avoid concomitant use	Potential largeν statin level Avoid concomitant use

ARV	NVP	EFV	LPV/r	NFV	SQV
Atorvastatin	No data	πAtorvastatin AUC by 43% EFV level unchanged Adjust atorvastatin dose according to lipid response, not to exceed maximum recommended dose	νAtorvastatin AUC 5.88 fold Use lowest possible starting dose with careful monitoring	νAtorvastatin AUC 74% Use lowest possible starting dose with careful monitoring	νAtorvastatin level by 450% when use as SQV/RTV Use lowest possible starting dose with careful monitoring
Pravastatin	No data	No data	νPravastatin AUC 33% No dose adjustment needed	No data	πPravastatin level by 50% No dose adjustment needed
Anticonvulsants					
Carbamazepine, Phenobarbital, phenytoin	Unknown. Use with caution Monitor anticonvulsant levels	Use with caution. One case report showed low EFV levels with phenytoin Monitor anticonvulsant and EFV levels	νCarbamazepine from RTV Both phenytoin and LPV/r levelsπ For all, avoid concomitant use or monitor LPV/ anticonvulsant levels	Unknown but may decrease NFV level substantially Monitor NFV/ anticonvulsant levels	Unknown for unboosted SQV but may markedly πSQV level Monitor SQV/ anticonvulsant levels
Proton pump inhibitors. All the PIs and EFV can increase levels of cisapride and non sedating antihistamines (aztemizole, terfenedine) which can cause cardiac toxicity. Co administration is not recommended					

Abbreviations: AUC: area under the curve, Cmax: maximum concentration, Cmin: minimum concentration.

Note: Concomitant use of fluticasone with RTV results in significant reduced serum cortisol concentrations. Coadministration of fluticasone with RTV or any RTV-boosted PI regimen is not recommended unless the potential benefit outweighs the risk of systemic corticosteroid side effects.

(Adapted from the Guidelines for the use of antiretroviral agents in HIV infected Adults and Adolescents, May 4, 2006, www.aidsinfo.nih.gov.)

6 Annex

Summary of Methadone and ART

Methadone is part of the WHO essential drug list and is being considered for OST use in India.

Administration of methadone with EFV, NVP or RTV decreases plasma levels of methadone, which may precipitate opiate withdrawal. Patients receiving methadone and commencing ART may require increased doses of methadone.

ARV dose adjustments in patients receiving methadone: Methadone withdrawal syndrome include signs and symptoms of methadone withdrawal typically occur 4–8 days after starting NNRTI-based ART and include chills, sweating, nausea, diarrhoea, abdominal cramping, rhinorrhoea, myalgia and anxiety. Patients receiving methadone replacement therapy and NNRTI-based ART require a step-wise increase in the daily dose of methadone of 5–10 mg until they are comfortable. Precipitating methadone withdrawal may trigger relapse to heroin use, distrust of medical providers, and unwillingness to take ART.

Contraindications for methadone are:

- Known hypersensitivity to methadone
- Acute asthma
- Alcoholism (unstable alcohol use)
- Use of MAOI anti depressants
- Severe hepatic impairment
- History of biliamy or renal tract spasm (relative contraindication)

Drug interactions between methadone and ARVs

ARV	Effect On Methadone	Effect On ARV	Comments
NNRTIs			
Efavirenz (EFV)	Methadone concentrations significantly decreased Methadone withdrawal common	Unknown	Observe for signs of methadone withdrawal and increase dosage as necessary Considerable increase in Methadone dose up to 50% commonly required
Nevirapine (NVP)	Methadone concentrations significantly decreased Methadone withdrawal common	NVP unchanged	
NRTIs			
Zidovudine (AZT)	None reported No dosage adjustments necessary	Concentrations increased Clinical significance unclear Adverse events possible	Monitor for adverse events of AZT Monitor for anaemia, neutropenia, nausea, myalgia, vomiting and headache
Lamivudine (3TC)	None reported	None reported	No known interactions
Emtricitabine (FTC)	Not studied	Not studied	No known interactions

Drug interactions between methadone and ARVs			
ARV	**Effect On Methadone**	**Effect On ARV**	**Comments**
Tenofovir (TDF)	None reported	None reported	No known interactions
Stavudine (d4T)	None reported No dosage adjustments necessary	Concentrations decreased	No dose adjustment of d4T required
Abacavir (ABC)	Methadone levels slightly decreased Risk of opiate withdrawal low Dosage adjustments unlikely but some patients might require increase in methadone dose	Concentrations decreased	Risk of opiate withdrawal low Methadone dose adjustment might be needed No dose adjustment of ABC required
Didanosine (ddI) **Buffered tablet** **Enteric-coated (EC) capsule**	None reported No dosage adjustments necessary	Concentrations significantly decreased when buffered tablet taken, but not with EC capsule	Avoid use of ddI buffered tablets Use EC capsule if available
PIs			
Lopinavir/ritonavir (LPV/r)	Methadone levels decreased	None reported	Opiate withdrawal may occur May require increase in methadone dose
Saquinavir (SQV)	Methadone slightly decreased when co-administered with SQV/RTV 400/400 BID	No change	No dose adjustment with this PI regimen, but monitor and titrate to methadone response as necessary
Ritonavir (RTV)	Methadone levels decreased	None reported	Studies limited Observe for signs of methadone withdrawal
Nelfinavir (NFV)	May decrease methadone levels	No dose adjustment required	Opiate withdrawal rarely occurs May require of methadone dose.

Interactions between methadone and other drugs			
Drug	**Indication**	**Effect On Methadone**	**Comments**
Rifampicin	Tuberculosis	Significant decrease in methadone levels May induce methadone withdrawal	Increase in methadone dose required if withdrawal symptoms present
Sertraline	Antidepressant	Increase in methadone levels	Associated with cardiac rhythm disturbances, caution when used with methadone
Carbamaze-pine and phenytoin	Anticonvulsants	Decrease in methadone levels and may cause opioid withdrawal	Increase in methadone dose may be required
Fluconazole	Antifungal	Increase in methadone levels (35%)	Clinical significance unknown

Physicians should discuss potential drug interactions with patients receiving methadone before initiating ARV therapy. Report all prescribed ART-related drug changes for patients receiving methadone to the patient's OST programme. Monitor for symptoms of withdrawal and/or excess sedation when ARV therapy is initiated or changed.

7 Annex

Patient Information Sheets: Treatment Education Cards

(To be translated at state level)

From: Adherence to Treatment for HIV: A Training Curriculum for Counselors, Engender Health 2006

Source: World Health Organization (WHO), 2005 March. Chronic HIV Care with ARV Therapy. Integrated Management of Adolscent and Adult Illnesses. Interim Guidelines for Health Workers at Health Center or Clinic at District Hospital Outpatient Draft. Rev. 1

1. TREATMENT EDUCATION CARD: d4T-3TC-NVP

Now you are on ART

	d4T-3TC-NVP		
	Stavudine	**Lamivudine**	**Nevirapine**
	Day 1-14	**Day 15 onwards**	
	**Morning:** Staudine Lamivudine Nevirapine	**Morning:** Staudine Lamivudine Nevirapine	
	**Evening:** Stavudine Lamivudine	**Evening:** Stauvdine Lamivudine Nevirapine	

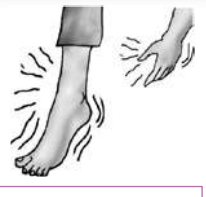
Remember that:

- If you miss doses (even 2 doses in a month) **DRUG RESISTANCE** can develop. This is bad for you and your community. (These drugs will stop working.)
- Drugs must be taken twice daily, **and miss no doses**.
- This is very important to maintain blood levels so ART can work.
- If you forget a dose, do not take a double dose.
- If you stop you will become ill within months or year.
- Drugs **MUST NOT** be shared with family and friends.
- If you find it difficult taking your pills twice daily, DISCUSS with health workers. ASK for support from your Treatment supporter, family or friends.

It is common to have side effects. They usually go away in 2–3 weeks.

If you have:	Do the following:
Nausea	Take the pill with food.
Diarrhoea	Keep drinking and eating

If Nausea or diarrhoea persist or get worse, or you have any of the following, report to the health worker **AT THE NEXT VISIT**.



- Tingling, numb or painful feet or legs or hands.
- Arms, legs, buttock, and cheeks become THIN.
- Breasts, body, back of neck become FAT

SEEK CARE URGENTLY IF:

- Severe abdominal pain
- Yellow eyes along with high fever, headache running nose and body ache
- Skin rash, along with fever and ulcer in the mouth and lips..

2. TREATMENT EDUCATION CARD: AZT-3TC-NVP

Now you are on ART

	AZT-3TC-NVP		
	Zidovudine	**Lamivudine**	**Nevirapine**

	Day 1- 14	**Day 15 onwards**
	**Morning:** Zidovudine Lamivudine Nevirapine	**Morning:** Zidovudine Lamivudine Nevirapine
	**Evening:** Zidovudine Lamivudine	**Evening:** Zidovudine Lamivudine Nevirapine

Remember that:

- If you miss doses (even 2 doses in a month) **DRUG RESISTANCE** can develop. This is bad for you and your community. (These drugs will stop working.)
- Drugs must be taken twice daily, **and miss no doses**.
- This is very important to maintain blood levels so ART can work.
- If you forget a dose, do not take a double dose.
- If you stop you will become ill within months or year.
- Drugs **MUST NOT** be shared with family and friends.
- If you find it difficult taking your pills twice daily, DISCUSS with health workers. ASK for support from your Treatment supporter, family or friends.

It is common to have side effects. They usually go away in 2–3 weeks. If you have them, do the following:

If you have:	Do the following:
Nausea	Take the pill with food.
Diarrhoea	Keep drinking and eating
Muscle pain, fatigue	These will go away.

If Nausea or diarrhoea persist or get worse, report to the health worker **AT THE NEXT VISIT**.

SEEK CARE URGENTLY IF:

- Severe abdominal pain
- Yellow eyes along with high fever, headache running nose and body ache
- Skin rash, along with fever and ulcer in the mouth and lips.
- Pale or do not have enough blood
- Fatigue and shortness of breath.

Note: Zidovudine, ZDV is also called AZT

3. TREATMENT EDUCATION CARD: AZT-3TC-EFV

Now you are on ART

AZT-3TC-EFV		
Zidovudine	**Lamivudine**	**Efavirenz**

	Daily
	**Morning:** Zidovudine Lamivudine
	**Evening:** Zidovudine Lamivudine Efavirenz

Remember that:

- If you miss doses (even 2 doses in a month) **DRUG RESISTANCE** can develop. This is bad for you and your community. (These drugs will stop working.)
- Drugs must be taken twice daily, **and miss no doses**.
- This is very important to maintain blood levels so ART can work.
- If you forget a dose, do not take a double dose.
- If you stop you will become ill within months or year.
- Drugs **MUST NOT** be shared with family and friends.
- If you find it difficult taking your pills twice daily, DISCUSS with health workers. ASK for support from your Treatment supporter, family or friends.

It is common to have side effects. They usually go away in 2 weeks. If you have them, do the following:

If you have:	Do the following:
Nausea	Take the pill with food.
Diarrhoea	Keep drinking and eating
EFV can cause brain effects such as sleepiness, dizziness, bad drams, or problems with sleep or memory	These side effects usually go away. Taking the efavirenz at night is important. Do not take efavirenz immediately after eating, it is best when take before sleep
Muscle pain, fatigue	These will go away

If nausea or diarrhoea persist or brain effects get worse, report to the health worker **AT THE NEXT VISIT**.

SEEK CARE URGENTLY IF:

- Bizarre thoughts/confusion
- Yellow eyes with high fever, headache running nose and body ache
- Skin rash, along with fever and ulcer in the mouth and lips
- Pale or do not have enough blood
- Fatigue and shortness of breath
- Missed periods/possibility of pregnancy

Note: Zidovudine, ZDV is also called AZT

4. TREATMENT EDUCATION CARD: d4T-3TC-EFV

Now you are on ART

d4T-3TC-EFV		
Stavudine	**Lamivudine**	**Efavirenz**

	Daily
	**Morning:** Stavudine Lamivudine
	**Evening:** Stavudine Lamivudine Efavirenz

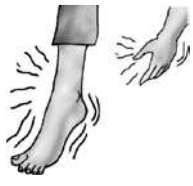
Remember that:

- If you miss doses (even 2 doses in a month) **DRUG RESISTANCE** can develop. This is bad for you and your community. (These drugs will stop working.)
- Drugs must be taken twice daily, **and miss no doses**.
- This is very important to maintain blood levels so ART can work.
- f you forget a dose, do not take a double dose.
- If you stop you will become ill within months or year.
- Drugs **MUST NOT** be shared with family and friends.
- If you find it difficult taking your pills twice daily, DISCUSS with health workers. ASK for support from your Treatment supporter, family or friends.

It is common to have side effects. They usually go away in 2 weeks. If you have them, do the following:

If you have:	Do the following:
Nausea	Take the pill with food.
Diarrhoea	Keep drinking and eating
EFV can cause brain effects such as sleepiness, dizziness, bad dreams, or problems with sleep or memory	These side effects usually go away. Taking efavirenz at night is important. Do not take efavirenz immediately after eating, it is best when take before sleep.

If Nausea or diarrhoea persist or brain effects get worse, or you have any of the following, report to the health worker **AT THE NEXT VISIT**.



- Tingling, numb or painful feet or legs or hands.
- Arms, legs, buttock, and cheeks become THIN.
- Breasts, body, back of neck become FAT

SEEK CARE URGENTLY IF:

- Bizzare thoughts/confusion
- Yellow eyes with high fever, headache running nose and body ache
- Skin rash, along with fever and ulcer in the mouth and lips
- Severe abdominal pain
- Missed periods/possibility of pregnancy

8 Annex

Checklist for Adherence Counseling

Reference: HIV Counselling Training Modules for VCT, PPTCT and ART Counsellors, NACO 2006

ADHERENCE COUNSELLING CHECKLIST 1

Counselling Session 1

Name of the Client .....

Date of counselling session .....

Assess of patient		
Medical history Knowledge of HIV/AIDS Prior use of ART Determine the social support Disclosure—have they disclosed to anyone? Alcohol/drug use Mental state		
Review the health status		
Ols CD4/viral laod		
Review living conditions and employment		
Housing Employment/income		
Describe the treatment programme and importance of adherence		
Drug regimen—name/frequency/storage/deitary instructions/not to share pills What ART does—suppresses virus/improves immunity/lessens Ols/not a cure Cost Side-effects and what to do Follow-up Importance of adherence and consequences of non-adherence		
Discuss adherence promotion strategies		
Buddy reminder—discuss role of support person Pill diary Other reminder cues		
Identity barriers to adherence	**Yes**	**No**
Poor communication Low literacy Inadequate understanding about HIV/AIDS Lack of social support Failure to disclose the HIV-positive status Alcohol and drug use Mental state		

ADHERENCE COUNSELLING CHECKLIST 2

Counselling Session 2

Name of the Client .....

Date of counselling session .....

Review client's understanding of HIV/AIDS
What is HIV and AIDS? What are opprtunistic infections? What do they understand by CD4 counts/viral load? What are the effects of treatment?
Review the treatment programme and importance of adherence
Drug regimen Dummy pill demonstration What ART does—improves immunity/lessens Ols/ART is not a cure? Need for continued prevention—use of condoms Side-effects and what to do Follow-up Importance of adherence and consequences of non-adherence
Review proposed adherence promotion strategies
Buddy reminder—discuss the role of a support person Review all pill diary Other reminder cues—HAART
Review barriers to adherence and the progress made so far
Poor communication skills Low levels of literacy Inadequate understanding about HIV/AIDS Lack of social support Failure to disclose the HIV-positive status Alcohol and drug use Mental state
Take the client's address and establish contact system with a treatment centre
Schedule the next counselling session and complete the appointment card

ADHERENCE COUNSELLING CHECKLIST 3

Counselling Session 3

Name of the Client .....

Date of counselling session .....

Assess the client's understanding of the disease and readiness to start
What is HIV disease? What are opprtunistic infections? What is meant by CD4 counts/viral load? What are the effects of treatment? What is their level of commitment of adherence
Review the treatment programme and importance of adherence
Drug regimen Dummy pill demonstration What ART does—improves immunity/lessens Ols/ART is not a cure? Need for continued prevention—condoms use Side-effects and what to do Follow-up Link between adherence and successful outcome
Review proposed adherence promotion strategies
Buddy reminder—discuss the role of a support person Review the pill diary Other reminder cues—HAART
Fill the ART register, schedule the next appointment and complete the appointment card
Refer to the Pharmacy/Chemist

9 Annex

Barriers to Adherence and ways to Address them

List of Barriers to adherence and ways to address them

1. Communication difficulties (language, cultural differences, patient attitudes regarding treatment efficacy, lack of comprehension about treatment plan or regimen)
   (i) Discuss in an open and non-judgemental way
   (ii) Provide patients with scientific basis for treatment
   (iii) Repeat and paraphrase
   (iv) Use counsellors who speak the same language and understand the cultural context of the patient
2. Literacy levels
   (i) Verbal repetition of adherence message, treatment plan and regimen
   (ii) Use patient literacy materials
   (iii) Use dummy pills for demonstration
   (iv) Review information with patient
3. Inadequate knowledge or awareness about HIV disease
   (i) Provide patients with scientific information about HIV disease
   (ii) Review Information with patients
   (iii) Use examples
4. Inadequate understanding about effectiveness of medications
   – Inform patients and bring change in attitudes and understanding of effectiveness of medications
5. Lack of social support
   (i) Establish contact with PLHA support groups
   (ii) Link with community health workers and home-based care services
   (iii) Link with charitable institutions, faith-based organizations
6. Discomfort with disclosure of HIV status
   (i) Counselling patient to support disclosure
   (ii) Identify other support persons such as friends or peers if patient unable to disclose to the family.
7. Difficult life conditions (lack of income, housing, food, support for childcare)
   (i) Establish contact with PLHA support groups
   (ii) Link with community health workers and home-based care services
   (iii) Link with charitable institutions, church programmes
8. Alcohol and drug use
   (i) Counselling—emphasize link between alcohol, ARV drugs and liver damage
   (ii) Family support
   (iii) Peer group support programmes, church programmes
   (iv) Medical consultation—de-addiction programmes
9. Depression and other psychiatric problems
   – Refer to physician for treatment
10. Negative or judgemental attitude of providers
   – Training of providers
11. System barriers (drug stock-out, shortage of staff, health facility closed)

10 Annex

Occupational Exposure Management-sample Flow Chart

Services provided	Day 0*	Day 3**	Week 4	Month 3	Month 6
1. Immediate management steps					
• First aid	X				
• Reporting to designated PEP officer	X				
• Risk assessment	X				
2. PEP discussion					
• Discuss PEP#	X				
• Obtain informed consent	X				
• Give first dose of PEP medication if required	X				
3. Source assessment					
• Consent for HIV test or information on HIV treatment history	X				
• Rapid testing if available	X				
• Risk assessment—consider window period, population prevalence, risk behaviour	X				
4. PEP prescription					
• PEP eligibility confirmation	X				
• Assess prior HIV risk	X				
• Dispense PEP medications	X	X (if 3-day starter pack given)			
Adherence counselling					
• Side effect counselling					
• Informed consent for PEP	X				
• Consider pregnancy	X		X		
• Arrange special leave from duty (2 weeks initially)	X X	X X			
5. HIV testing and counselling					
• Crisis counselling	X				
• HIV counselling and testing with informed consent (with further visit for results when available)##	X	X (if not done on day 0)	X	X	X (If PEP taken)
• Consider counselling/support for significant others	X	X	X	X	
• Advice on prevention of transmission	X	X			

Services provided	Day 0*	Day 3**	Week 4	Month 3	Month 6
6. Laboratory testing					
• Other testing as appropriate, eg					
– Pregnancy test	X		X		
– HBV and/or HCV antibody test	X			X	X
– Haemoglobin	X		X		
7. Follow up					
• Ongoing support		X	X	X	X
• Referrals, as appropriate	X	X	X	X	X
• Symptom review		X	X	X	
• Occupational health and safety review		X			

* On presentation – up to 72 hours
** If 3 day starter pack given *(change time as per local protocol – 7 days or 14 days)*
# If low risk exposure, or if PEP declined, offer services in points 3, 5 and 7 only
HIV Testing at 6 weeks for seroconversion

11 Annex

Form A1— AEB Medical Notification Form

Accidental Exposure to Blood—Medical Notification Form (revised 2006)

(This is a confidential form to be filled in by the designated officer for PEP and to be used for medical referral purposes. This should be kept in file by the institute which manages the PEP.)

Details of the Exposed Person
S.No……

Name: ..... Age ..... Gender: Male/Female .....

Details of the Exposure

Date of exposure: ..... Time (exact): .....

Place : .....

Time (hours) since exposure:

❒ < 2 hours ❒ between 2 and 24 hours ❒ > 24 hours ❒ 72h ❒ longer (specify): .....

Contact with: ❒ blood ❒ any other body fluid

(specify): .....

Type of contact : Needle-stick/Mucosal/Intact skin/Mucocutaneous/Others (specify):

If the exposure involved a needle, specify: ❒ hollow needle ❒ plain needles Size of needle: ….....

.....

.....

Description of the circumstances of the accident:

.....

.....

Description of the wound:

.....

.....

Information of the source person

Is the source person known? ❒ Yes ❒ No

If Yes, results of the medical/lab assessment (HIV status if available, HBV, HCV):

.....

.....

Steps taken after the exposure

First aid (specify) .....

Prophylactic treatment: Advised ❒ yes ❒ no

Prescribed ❒ yes ❒ no

PEP regimen: Basic/Expanded (specify) .....

.....

HBV vaccination given: Yes/ No (specify) .....

Investigations results (HIV-Ab baseline, HCV, HBsAg , Pregnancy test etc) .....

.....

PEP completed (4 weeks): Yes/ No (specify reason) .....

Side effects to PEP drugs: .....

Other treatment/referrals given.....

Outcome of the exposed person

At 3 months: HIV negative/positive Date of test .....

At 6 months: HIV negative/positive Date of test .....

Others .....

Remarks:

Signature ..... Place ..... Date .....

(ART nodal officer/Infection control officer/Physician responsible for exposed person)

12 Annex

Form A2—PEP Informed Consent/Refusal Form

PEP Informed Consent/Refusal Form

When PEP has been advised this form should be filled in and signed by the exposed person, and signed by the designated officer for PEP. This should be kept in the file with Form A1.

Name: .....

Date of birth: ..... Sex: .....

Date of the accidental exposure: .....

I, the undersigned, ..., hereby declare:

- That I have been informed of the recommendations with regard to prophylactic treatment after accidental exposure to HIV.
- That I understand the risk of transmission after accidental exposure to blood.
- That I have been informed of the effectiveness and the possible side- effects of this treatment.

I have been offered prophylactic treatment, and:

❒ I have decided not to take it.

❒ I agree to follow this prophylactic treatment for a period of 28 days and I agree to accept medical supervision for this.

Date:.....

Signature of the exposed person: .....

Signature of the designated officer: .....

13 Annex

Information Sheet for Health Care Providers on Post-exposure Prophylaxis (PEP) and Follow-up after an Accidental Exposure to Blood (AEB)

This is to be given to the exposed person, for information only.

The doctor assessed that there is a risk of transmission of HIV infection as a result of this accidental exposure and that you can start antiviral prophylaxis, if you agree.

1. You must understand that this preventive medication (PEP):
   - Must be started, if possible, within 2 hours of the accidental exposure (within 72 hours at the latest) for maximum benefit
   - Although there is strong evidence that PEP may prevent infection with HIV, but this preventive intervention is not 100% effective.
   - May cause minor side-effects (as with any medication), especially digestive problems, headache, fatigue, malaise, muscle ache or joint ache
   - Must be taken regularly in two doses per day for 4 weeks (28 days)
   - Must be backed up by regular laboratory check-up
   - Requires the use of condoms during the period of PEP treatment until the results of the HIV testing at 3 months are known
   - Requires the use of efficient contraception during the period of treatment until the results of the HIV test at 6 months are known
   - If you stop taking PEP at any time, you will not get the full benefit of the medication
   - It is your choice whether or not to take PEP. You will be asked to sign a consent form.
2. The following is proposed as laboratory investigations and follow-up, if you agree:

Timing	In persons taking PEP (standard regimen)	In persons not taking PEP	Follow-up dates
Baseline (within 8 days after AEB)	HIV Hepatitis B and C Complete blood count Liver function test	HIV Hepatitis B and C	
Week 2 and 4	Liver function test Complete blood count	clinical monitoring for hepatitis	
Week 6	HIV	HIV	
Month 3	HIV Hepatitis B and C Liver function test	HIV Hepatitis B and C	
Month 6	HIV Hepatitis B and C Liver function test	HIV Hepatitis B and C	

14 Annex

Form A3: Monthy Report to SACS

Monthly Report of Occupational Exposure in State

(Send this form to SACS/NACO monthly)

A photocopy of form A1 (with names blacked out) is to be sent along with Form A3 to SACS/NACO for every PEP given by the hospital at the end of 6 months.

SACS .....

Reporting officer name.....

No.	Institution	Number of cases requesting for PEP	Number of cases prescribed PEP	Regimen given (basic/expanded)

15 Annex

Risk Assessment Guide for the Source Patient

The following points need to be covered when questioning and examining the source patient.

These need take into consideration the local HIV epidemiology, clinical and cultural conditions.

There is no such thing as a "score" in this regard—it is up to the doctor to interpret the results of the clinical assessment.

It is important that questioning be conducted in a way that reveals relevant events that may have occurred several years ago:

1. **Family history**: Have any family members recently been ill or died. What was the cause?
2. **Recent personal history of HIV acute infection symptoms** (generally appear 3 to 6 weeks after infection): general lymphadenopathy (predominantly in the cervical and axillary areas); fever of unknown origin; muscular cramps, joint pain; skin rash, urticaria; oral and genital ulcers.
3. **Individual's personal "risk history" of HIV**
   - Has the source person ever had a blood transfusion? If so, under which conditions?
   - Has the source person had injections or surgical procedures (including any traditional scarification) with non-sterile/reusable clinical material?
   - Is the source person an injecting drug user and does s/he possess injection material?
   - Does the source person belong to a population group considered at risk? For example: sex worker, truck driver; migrant worker; soldier, men who have sex with men…
   - Is the source person involved in high-risk sexual activities? Example: practising unsafe sex with multiple partners; already treated or undergoing treatment for a sexually transmitted disease; having sexual partners of a person in any of the above categories.
4. **Suspicion or actual presence of symptoms and/or HIV infection within the previous six months or more** : tuberculosis; continuous or intermittent fever; chronic diarrhoea; weight loss; chronic cough lasting longer than a month; skin infections (severe and/or recurrent); oral thrush; night sweats.
5. **Clinical examination findings**
   - Cardinal signs: Kaposi sarcoma; Pneumocystis Jiroveci (carinii) pneumonia; cerebral toxoplasma; oesophageal candidiasis; cytomegalovirus retinitis.
   - Characteristic signs: oral thrush; hairy leukoplakia of the tongue; Cryptococcal meningitis; pulmonary or extra-pulmonary tuberculosis; herpes zoster - particularly multi-dermatomal; severe prurigo; high-grade B-cell extranodal lymphoma.
   - Associated signs: weight loss (recent, unexplained) of more than 10% of initial body weight; fever (continuous or intermittent) for longer than a month; diarrhoea (continuous or intermittent) for longer than a month; ulcers (genital or perianal) for more than a month; cough lasting longer than a month;
     neurological complaints or findings; generalised lymphadenopathy (extra-inguinal lymphatic areas);
     reactions to drugs (not previously observed); skin infections (severe and/or recurrent): e.g. warts, dermatophytes, folliculitis. lymphopenia (known).
6. Past history of any long term medical treatment (eg anti-TB treatment, antiretroviral therapy)

List of Physicians for Advice on HIV/AIDS Clinical Management and PEP

No.	Name of the centre	Contact person	E-Mail	Mobile no.	Other contact numbers
1	NACO	Dr. B B Rewari	drbbrewari@yahoo.com	09811267610	
2	GHTM, Tambaram	Dr. S. Rajasekaran	Rajasekaran.S@GHTM.com	09444013672	
3	CMC, Vellore	Dr. Dilip Mathai Dr. O. C Abraham Dr. Anand Zachariah	dilipmathaiidtrc@yahoo.co.in or med1@cmcvellore.ac.in	09443336984	0416-2282089
4	K. E. M. Medical College Hospital, Mumbai	Dr. A. R. Pazare	arpazare@hotmail.com	09820572212	
5	Sir JJ Hospital, Mumbai	Dr Alaka Despande	alakadeshpande@rediffmail.com	09869168886	022-23703696
6	BJ Medical College, Ahmedabad	Dr. Bipin K. Amin	bipin_dr@yahoo.com	09879208979	
7	BJ Medical College, Pune	Dr. A L Kakrani	kakrani@hotmail.com	09422004669	020-26128000 - ext 312 (O) 020-26120718 (Fax)
8	King George Medical University, Lucknow	Dr. A. K. Tripathi	tripathiak2005@hotmail.com	09415115599	
9	BHU, Varanasi	Dr. Shyam Sundar	drshyamsundar@hotmail.com	09415228390	
10	School of Tropical Medicine, Kolkata	Dr. S. K. Guha	drskguha@vsnl.net or drskguha@rediffmail.com	09831234802	033-2241-4900/ 4065/4429 (O)
11	PGI, Chandigarh	Dr. Ajay Wanchu	awanchu@yahoo.com	-	0172-2756678 0172-2756979
12	JN Hospital, Imphal	Dr. K. Priyokumar	artjnh@rediffmail.com or dr_priyokumar@rediffmail.com	09436029192	
13	WHO, India	Dr. Po-Lin Chan (for queries on guidelines for adults/children/ PPTCT/PEP)	chanpl@searo.who.int	-	011-42595600 (O) 011-23382252 (Fax)

* This list will be updated regularly. Refer to www.nacoonline.org

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