BELIZE 2018

THE NATIONAL HIV GUIDELINES

CLINICAL MANAGEMENT GUIDELINES FOR HIV/AIDS

National TB, HIV/AIDS & other STIs Program

Ministry of Health

Belize

2018

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List of Acronyms

3TC	lamivudine
ABC	abacavir
ABG	arterial blood gases
AIDS	acquired immunodeficiency syndrome
ALT	alanine aminotransferase
ANC	antenatal clinic
ART	antiretroviral therapy
ARV	antiretroviral
AST	aspartate aminotransferase
ATV	atazanavir
AZT	zidovudine (also known as ZDV)
BID	twice daily
BMI	body mass index
BPI	boosted protease inhibitor
CD4	cell T-lymphocyte bearing CD4 receptor
CMV	cytomegalovirus
CNS	central nervous system
CXR	chest X-ray
DBS	dried blood spot
ddI	didanosine
DNA	deoxyribonucleic acid
DRV	darunavir
DRV/r	darunavir/ritonavir
DTG	daltegravir
EC	enteric-coated
EFV	efavirenz
ETV	etravirine
EPTB	extrapulmonary tuberculosis
FBC	full blood count
FDC	fixed-dose combination
FPV	fos-amprenavir
FTC	emtricitabine
Hb	hemoglobin
HBV	hepatitis B virus
HCV	hepatitis C virus
HDL	high-density lipoprotein
HIV	human immunodeficiency virus
HIVDR	HIV drug resistance
HIVRNA	human immunodeficiency virus ribonucleic acid

HSV	herpes simplex virus
IDV	indinavir
INH	isoniazid
IRIS	immune reconstitution inflammatory syndrome
LPV	lopinavir
LPV/r	lopinavir/ritonavir
PMTCT	Prevention of mother-to-child transmission (of HIV)
NNRTI	non-nucleoside reverse transcriptase inhibitor
NRTI	nucleoside reverse transcriptase inhibitor
NVP	nevirapine
OI	opportunistic infection
PCP	*Pneumocystis jiroveci* pneumonia
PEP	Post-exposure prophylaxis
PI	protease inhibitor
PLWH	People living with HIV
PML	progressive multifocal leukoencephalopathy
PMTCT	prevention of mother-to-child transmission (of HIV)
PrEp	Pre-exposure prophylaxis
/r	low-dose ritonavir
RAL	raltegravir
RBV	ribavirin
RNA	ribonucleic acid
RT	reverse transcriptase
RTI	reverse transcriptase inhibitor
RTV	ritonavir
Sd-NVP	single-dose nevirapine
SJS	Stevens-Johnson syndrome
SQV	saquinavir
TB	tuberculosis
TDF	tenofovir disoproxil fumarate
TEN	toxic epidermal necrolysis
TLC	total lymphocyte count
VL	viral load
ULN	upper limit of normal
UNAIDS	Joint United Nations Program on HIV/AIDS
WBC	white blood cell count
WHO	World Health Organization

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Foreword: My friends,

The government of Belize remains committed through its Ministry of Health, and thanks all its partners for their unwavering support, and meaningful involvement in the integration of services that have positively impacted the control, and further spread of HIV in Belize. This positive outcome in our country is evidenced by a plateau in the number of new cases being diagnosed yearly within the last 5 years. This tremendous achievement signals that with more precise and consolidated efforts we can also eliminate the mother to child transmission of HIV in Belize.

This newly revised and updated national HIV guideline contains a standardized set of essential steps for the clinical management, monitoring and follow up of PLWH who are on ART (antiretroviral therapy) and their response to treatment. This much expected guideline will be used objectively in sensitizing healthcare workers in general with new evidence in the care and treatment of persons with HIV/AIDS. This 2018 manual includes newer evidence based recommendations that are in line with that of other international guidelines, including that of WHO/PAHO and has been adapted to our Belizean reality.

The guideline continues to build and reflects my government's commitment to the provision of free, highly effective anti-retroviral therapy, along with much needed test that monitor response to treatment such as CD4 and viral load. The Ministry therefore seeks to strengthen and build further capacity in clinical management, scaling up much needed essential skills for the treatment of those affected with HIV in Belize.

It is the intention of the Ministry to sensitize and build capacity in HIV care immediately across the width and breathe of our country. Therefore as we mature as a nation, our actions must be more dynamic with the change of time to support newer efforts to ensure a sustainable response to care and treatment within the public health arena. At this point in the epidemic we must improve our skills, challenge ourselves, and work relentlessly with professionalism, mutual respect, as we deliver care of those affected by HIV. I therefore extend and express a sincere gratitude to those committed to the care of those with HIV/AIDS in our jewel, and ask that we continue to work in unity as one Belize for our brothers and sisters. This new guideline is another example of our national response in the fight against HIV/AIDS epidemic in Belize.

With thanks,

Hon. Pablo Marin,

Minister of Health

Introduction

The year 2003 has been hallmarked as an unforgettable era with the Government of Belize through the Ministry of Health providing and implementing a much needed strategy by introducing free ART for persons affected and living with HIV in Belize. This major step was also accompanied by laboratory strengthening of local capacity in testing and monitoring clinical improvement for those on ARVs.

This final review includes elements and makes reference to the 2016 WHO/PAHO clinical management guidelines, and other prestigious norms. This standardized norm focuses not only on the adult and adolescent populations but also includes the clinical management of HIV/AIDS in the pediatric group.

The task of implementing these new guidelines requires efficient, high quality and reliable laboratory support services that includes, routine laboratory monitoring and specific test such as (CD4, viral load test).

The Ministry of Health National HIV program recommends that all HIV positive individuals be placed on HAART once diagnosed. However, the clinician must follow national guidelines and acertain that the persons is ready to accept treatment after a carefull and individualized assessment of his clinical status.

Objectives of the Guidelines

1. To provide a standardized set of criteria that will serve as guidance for the clinical care and treatment of adults, adolescents, and children infected with HIV.

Key Areas Updated in the Guidelines are included in the following sections:

- Comprehensive Care
- Preparation for Beginning Treatment
- When to Start?
- What to Start with ?
- Monitoring of Patients to evaluate impact
- Management of TB/HIV Co-infection
- Treatment Failure and when to Switch ARVs?
- Second and Third Line Regimens
- Co-infections and Opportunistic Infections care
- HIV and Non-infectious Co-morbidities
- Pre-Exposure Prophylaxis
- Post-Exposure Prophylaxis
- HIV Prophylaxis in Victims of Sexual Assault
- Pediatric HIV Care

Audit Standards

These guidelines have been developed to ensure that quality care and treatment is provided to all persons accessing HIV care and treatment. This guideline outlines the following points:

- All HIV positive patients should be referred to HIV care and treatment centers.
- During their first visit to the HIV care and treatment center, a complete history, physical examination and baseline laboratory testing (blood samples), must be conducted on all patients as per **Table 1.**
- All patients with HIV (including those on ART) should have a complete physical examination and pertinent clinical/laboratory investigations as indicated in **Table 2**.
- All patients should have adherence counseling at least twice per year.

- ❖ Patients initiating treatment should have a follow-up CD4 cell count test at least every 6 months. If adherence is maintained and consistent and evidenced by clinical improvement and his/her CD4 cell count level improves this can be done at least once a year.
- ❖ Patients initiating/or on treatment should have viral load testing at least every 6 months or once a year if the patient has undetectable levels (< 50 cells).

Comprehensive Care for PLWHA

The use of ART in the treatment of HIV/AIDS has resulted in a global reduction of the morbi- mortality rates in individuals affected by this epidemic. HIV/AIDS is now considered a chronic disease and not a fatal disease. The comprehensive care of PLWH should include: a proper psychosocial evaluation and support at the time of diagnosis, before starting ART and during the course of treatment. ART usually improves a patient's wellbeing and helps in preventing the development of opportunistic infections (OI), and/or progression to advanced immuno-suppression (CD4 cell count <200 cells/mm^3). More info see National HIV Guidelines

Treatment Preparedness:The main goal is to offer supportive counselling and education to a HIV positive person regarding his/her disease. This preparation maximizes long-term compliance, treatment adherence, enrolment in treatment. Factors that contribute to ART adherence includes:

1. low pill count
2. education on ART, its benefits and adverse effects
3. treatment readiness being directly linked with improved adherence to ART once it is initiated
4. Enrolment into care before the initiation of ART provides an opportunity for PLWH to learn, understand, and prepare themselves for successful lifelong ART treatment.

ART treatment must include all elements of comprehensive care to ensure proper adherence.

Tuberculosis (TB) /HIV Co-Infection

TB/HIV co-infection is one of the most frequent life-threatening and leading causes of death by an opportunistic infection in PLWH in Belize. Comprehensive care for TB/HIV involves the implementation of all TB/HIV collaborative activiites and most importantly the WHO three I's strategy:

- ❖ Isoniazid preventive treatment (IPT) where indicated,
- ❖ Intensified case finding (ICF) for active TB,
- ❖ and TB infection control (IC)

Note: All HIV positive patients should be regularly screened for TB and all TB patients should be tested for HIV. See National TB guidelines.

Co-trimoxazole prophylaxis (Cotrimoxazole preventative therapy CPT)

CPT is to be prescribed to all symptomatic individuals with:	1.WHO clinical stages 2-4 2. Pregnant women 3. Patients with a CD4 cell count of <350 cells/mm^3 4. HIV + FOR OIs Prevention 5 Persons with concomitant immune suppression 6.Persons taking (e.g. use of steroids > 20 mg prednisone per day for > 2 weeks,cancer

	chemotherapy, using biological agents like rituximab and others).

Assessment of HIV-infected Patients at Initial and Subsequent Visits

Initial visit -Table 1: Screening/Laboratory Testing (PRE-ART)

- Complete medical history
- Physical examination, including height, weight, BMI, blood pressure, waist circumference
- Screening for TB including symptomatic screening on every encounter, scrutinizing for the presence of cough, fever, weight loss and night sweats.
- Assessment of social and psychological condition with provision of support and counseling as needed
- Consideration of HBV vaccination (depending on serology results) and pneumococcal vaccination
- Assessment of sexual and reproductive health
- History of vaccination, travel and country of origin
- Assessment of sero-discordant couples and recommendation for the use of ART
- Laboratory testing as described in Table 2

Annually

- Physical examination
- Evaluation of social and psychological support
- Healthy lifestyle changes (nutrition, drug use, adverse lifestyle habits)
- Laboratory test as described in Table 2

Considerations in Laboratory Monitoring in Patients with ART (table 2)

- For NNRTI-containing regimens, monitoring of **liver enzymes** is recommended if signs and symptoms of ART related toxicity is evident. In women on NVP and CD4 count of 250−350 cells/mm^3, clinicians should monitor hepatic enzymes at weeks 2, 4 and 12 after initiation of ART.
- For AZT-containing regimens, **haemoglobin (Hb) measurement is recommended with close monitoring as they may develop signs/symptoms of anemia**. This is evident in those with low body weight and/or low CD4 cell counts. Hemoglobin levels must be monitored at 1 month after initiating AZT and every 3 months. **AZT should not be given if Hb is <7 g/dl**.

Table 1: Screening/Laboratory Testing (PRE-ART)and or baseline

Tests	Initial	6 Months	Annually
Confirmation of HIV positive antibody status	X		
Physical examination, including height, weight, BMI, blood pressure, waist circumference	X	X	X
CD4 count and % (optional: CD8 count and %)	X	X	X
HIV RNA (viral load)	X		X
Complete blood count	X	X	X
AST, ALT, Alk phosphatase, calcium, phosphate, creatinine clearance	X		X
Antibody tests for Hepatitis B, C and syphilis	X		X (if previously negative)
Fasting blood glucose and lipids to include total LDL & HDL cholesterol and triglycerides	X		X
Complete urinalysis	X		X
Cardiovascular risk assessment	X		X
Sexually Transmitted Infection (STI) screening (including anal swab)	X		X
PSA	X		
Cervical Pap smear	X		X

Adapted from the European guidelines for HIV/AIDS 2016

Table 2: Screening/Laboratory Monitoring (on ART)

Tests	Treatment Initiation	6 months	Annually
CD4 count and % (optional: CD8 count and %)	X	X	X
HIV RNA (viral load)	X		X
Complete blood count	X	X	X
AST, ALT, Alk phosphatase, calcium, phosphate, creatinine clearance	X	X	X
Antibody tests for Hepatitis B, C and syphilis HIV/HBV or HIV/HCV positive (perform liver function test at weeks (4, 12) after starting ART)	X		X (if previously negative)
Fasting blood glucose and lipids to include total LDL & HDL cholesterol and triglycerides	X	X	X
Complete urinalysis	X		X
Cardiovascular risk assessment (according to ART)	X		X
Sexually Transmitted Infection (STI) screening (including anal swab)	X		X
Cervical Pap smear			X

Adapted from the European Guidelines for HIV/AIDS 2016

Table 3: Monitoring ART in those at higher risk of adverse events

ARV drug	Major toxicity	High-risk situations*
AZT	Anemia Neutropenia	CD4 count of < 200 cells/mm^3 BMI < 18.5 (or body weight <50 kg) Anemia at baseline
TDF	Renal dysfunction	Underlying renal disease Age > 40 years BMI < 18.5 (or body weight < 50 kg) Diabetes mellitus Hypertension Concomitant use of a PI or nephrotoxic drugs
EFV	Teratogenicity	Use with caution in first trimester of pregnancy
	Psychiatric illness	Depression or psychiatric disease (previous or at baseline)
NVP	Hepatotoxicity	HCV and HBV co-infection

For TDF(Tenofovir)-containing regimens (monitor creatinine closely and calculate creatinine clearance on starting therapy and every 6 months. If this cannot be done it should not be a barrier to its use.

Assessing and Supporting Patient's Readiness to Start ART

The decision to start a person on ART should include: <u>the physician's clinical expertise and a careful assessment of each patient's barriers to adherence- ensuring comprehensive care</u>. Look out for Barriers to adherence such as:

Personal factors :

1. Depression
2. Alcohol or recreational drug use
3. Cognitive problems
4. Low literacy
5. Health beliefs (cultural and social backgrounds)
6. Lack of social support and disclosure.

Systemic factors:

1. Such as drug availability and supply
2. Access to care and treatment services.

Assessment and Support for Patients on ART

Assessment of adherence should be performed at every visit in order to identify and rectify any potential barriers. A trusting and non-judgmental relationship between the health care provider and the patient is critical in this regard. Two important methods of assessing adherence are the patient's recollection of missed doses and pharmacy refill records.

Some key strategies for promoting treatment adherence are:

- establishing trust (provide concise and, individualized information, do not allow ambivalence, assess the person's information needs and support his/her information seeking)
- closely monitor adherence at routine visits
- allow the patient time between visits for questions or to suggest solutions to problems
- involving patient's social network to provide ongoing adherence support
- adding adherence assessment and reinforcement to job descriptions of support team members, such as nurses, pharmacists, case managers, social workers and clinicians' assistants
- Reinforce the patient's decision and discuss integration into his/her daily life

The different stages of readiness to begin treatment. are as follows:Pre-contemplation, Contemplation, Preparation and Action see HIV Guidelines

When to start ARVs? Box 1: Recommendations on when to start antiretroviral treatment

1. **All individuals with confirmed HIV infection are eligible for ART, irrespective of CD4 cell count, WHO clinical stage, age, pregnancy or breastfeeding status, co-infection status, risk group, or any other criteria (a possible exception could be elite controllers with high and stable CD4 count). See note ****
2. **Optimizing complicance and adherence is a priority, so the person starting ARV's needs to be appropriately prepared.**
3. **Therapy with ART is recommended with any level of CD4 cell count in order to reduce sexual transmission, risk of AIDS event and mother to child transmission of HIV (before third trimester of pregnancy).**
4. **Attempts should be made to reduce the time between diagnosis and ART initiation to improve health outcomes.**
5. **Knowledge of preferred ART regimens for adults and adolescents allows for a reduced dosage of efavirenz to improve tolerability**

** Special consideration for ART initiation should be carried out in all HIV positive persons as defined by the Test and Treat

Antiretroviral Therapy (Adherence and Drug Resistance)

Treatment failure may result when a patient's strain of the HIV develops resistance to one or more of his/her antiretroviral medications.

Drug resistance may occur in the following situations:

- Insufficient drug dosage and/or potency
- The presence of preexisting mutant strains that are resistant to the medications administered to the patient.
- Drug resistance is also directly associated to poor adherence, but may also present itself in some patients with optimum and high levels of adherence: e.g. in a person with chronic diarrhea and malabsorption due to sub-therapeutic drug levels in the blood resulting in resistance.

Immunological Assessment:

ART should be initiated irrespective of the CD4 cell count level. The total lymphocyte count (TLC) is no longer used as a criteria for initiation of ART.

Virological Assessment:

Viral load testing is not a requirement for starting a patient on ART. VL testing is crucial in

1. Diagnosing treatment failure
2. Monitoring adherence
3. Evaluating response to treatment

The earlier virological failure is detected, the earlier clinicians can develop and implement targeted adherence interventions, thus preserving the efficacy of second line drugs regimens.

What to start? Table 5 recommended first line and and alternative first-line regimens for adults and adolescents .

Table 4: Table 5 recommended first line and and alternative first-line regimens for adults and adolescents

ARV Regimen First line ART in Belize	First line ART in Belize	Alternative fist line regimen
Adults/Adolescents	AZT+3TC+EFV TDF+FTC+EFV TDF+3TC+EFV	ABC +3TC +EFV
Pregnant /Breast Feeding	AZT+3TC+ LPV/r	

Source: Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection What's new? WHO. November 2015

Test and Treat Principle: All persons who have been recently diagnosed and have been clinically assessed (comprehensive care ensured) and are willing to start ARV treatment can be placed on the following ART regimen **see table 5.**

How to Monitor ART Response in HIV -Viral load testing (VL) is indispensable for diagnosing and confirming treatment failure. **Testing should be done at six (6) and twelve (12) months after initiating ART. If Viral suppression is evident VL can be done every 12 months**.

Adherence and HIV Resistance to ARV Therapy

Definition: Patients with HIV-VL >50 viral copies, after 6 months of starting ART (initiation or modification) will indicate the possibility of lack of adherence or possible resistance to ART. Note: Patients starting with ART with >100,000 viral copies may take longer than 6 months to achieve viral suppression.

Alternative:

The following criteria can be suggestive of lack of adherence and possible resistance

1. Persistent HIV-VL >1000 copies/ml (two viral loads measured within a 3 months interval with good compliance) or after at least 6 months of using the actual regimen

Viral Blips: maybe due to transient increase in viral load. These transient, low level increases are followed by return to suppression levels without any change in therapy. Proposed explanations for these fluctuations are: fluctuations in adherence, concurrent illnesses or vaccinations, artifacts due to variablility in the VL assay.

Source: Farmer A et al. Factors associated with HIV viral load "blips" and the relationship between self reported adherence and efavirenz blood levels on blip occurrence: a case control study. AIDS research and therapy. 13:16, 2016.

Factors associated with virological failure

1. Non-adherence to ARVs
2. Appearance of suspected, or new and/or recurrent HIV associated condition (WHO stage III/IV) which develops at least 6 months after initiating ART (excluding IRIS).

Note: There is low specificity and sensitivity when we use clinical and immunological criteria to identify virological failure. The use of viral load is essential on this issue.

ARV compliance MUST be properly evaluated before thinking of ART resistance. Evaluate for

1. patient drug tolerability
2. drug-drug interactions
3. drug-food interactions
4. existing psychosocial issues.

Drug resistance testing should be indicated if after carefuell ART review there is still:

1. suspicion of a failing therapy
2. patients with HIV-VL levels >1000 copies/ml
3. chronic HIV infection and history of the use of multiple regimen.

When to Switch ART

WHO emphasizes a public health approach on deciding and selecting a second and/or third-line ART.

Preferred second-line regimens and alternatives should be consistent with the following principles:

1. Availability of fixed-dose combinations
2. Tolerability and the risk of resistance mutation

The principles for the selection of third-line regimens are:

1. The regime should include new drugs with minimal risk of cross-resistance to previously used regimens

Patients on a failing second-line regimen with no new ARV options should continue with a tolerated regimen.

HIV/Tuberculosis (TB) Co-infection

TB is one of the leading causes of death in patients with advanced HIV infection. Failure to diagnose and treat TB disease promptly in PLWH may increase mortality and transmission in the community. TB disease spread quickly in congregate settings such as hospitals, homeless shelters, jails and prisons

Clinical Presentations of HIV-related TB

- The clinical presentation in PLWH with CD4 cell counts of > 350 cells/mm^3 is similar to that of TB among HIV negative persons
- TB is frequently limited to the lungs
- Common radiological findings but not specific include: upper lobe fibro nodular infiltrates with or without cavitation/s
- With increasing immunodeficiency, extra-pulmonary TB with or without pulmonary involvement maybe seen and be more common if CD4 cell-counts are lower than 50 cells/mm3
- TB may present itself as a systemic disease (high fevers, rapid progression and sepsis syndrome).

"Clinicians should NOT diagnose pulmonary TB in PLWH based on an abnormal chest X-ray, signs and symptoms of chest disease and negative sputum smears (several lung diseases can resemble PTB on X-ray and in signs and symptoms)." (Manual for the Prevention, Diagnosis, Treatment, Care and Control of Tuberculosis in Belize, 2016)

Diagnosis:

1. Screen all TB patients for HIV infection and all HIV seropositive for TB.
2. Obtain a detailed medical history and conduct a thorouogh physical examination ensure that you check for the following: present **cough, fever, weight loss, night sweats.**
3. **Ask for a C X Ray to be done if needed.**

HIV affects the progression of TB disease in the following ways:

A. May cause reactivation of LTBI to active disease in HIV positive individuals.This is preventable through the use of isoniazid preventive therapy (IPT).

B. May cause rapid progression from recent TB infection to active TB disease. Immunocompromised persons infected with TB bacilli from another patient may develop TB disease within weeks.

Isoniazid Preventative Therapy (IPT) and Recommendations

1. All Adults and adolescents living with HIV and that **DO NOT** have active TB treat with **isoniazid (IPT) for 9 months,** regardless of the CD4+ count, including those on ART, also those patients who have been previously treated for TB and pregnant women. IPT Dosage in Adults ---------- 5mg/kg (maximum 300 mg)
2. HIV positive patients > than 12 months of age, that **DO NOT** have active TB based on TB-Symptom-screening and have no contact with a TB case, provide **9 months of IPT**.
3. Children living with HIV and < than 12 months of age and contact of a person with active TB, but **does NOT** have active TB disease, should be treated with **IPT for 9 months**.
4. All adults and children living with HIV, who were treated and completed their treatment for active TB disease, should receive **Isoniazid for an additional 6 months**. INH at 5-10mg/kg.

5. The use of IPT in does not increase the risk of developing Isoniazid resistant TB and is not a valid reason to avoid IPT.

We must Rule out active TB before starting IPT in HIV positive persons!!!

IPT must NEVER be used in patients with HIV infection that have signs and symptoms consistent with active TB, or in patients in whom TB disease cannot be safely excluded.

TB and ART Drug Interactions

The concurrent use of ART and TB drugs may be complicated by the presence of drug toxicity, drug interactions, and the development of IRIS (immune reconstitution inflammatory syndrome). The prognosis of patients with HIV/TB co-infection improves with the use of ART. For more information see http://www.who.int/hiv/mediacentre/en) .

Management of HIV/TB Patients Who Fail to Respond to Antiretroviral Therapy

Principles of Antiretroviral therapy in adults and adolescents with co-infection are as follows:

- Clinicians must Start ART in PLWH with active TB irrespective of CD4 cell count
- TB treatment must be started first, followed by ART within the first 2 to 8 weeks of starting TB medication. CD4 cell counts more than 50 cells/mm^3)
- In patients with Co-infection and severe immunosuppression (CD4 cell counts less than 50 cells/mm^3) begin ART within the first 2 weeks of starting TB treatment.

ART Regimens for Patients Receiving TB Treatment

Efavirenz-containing regimens are the recommended first line of therapy for TB patients.

a. EFV + ZDV +3TC

b. EFV + TDF +FTC

Alternatives to EFV are needed in the following scenarios:

- Patients who are intolerant to Efavirenz
- Patients infected with a strain of HIV that is resistant to NNRTI's

Multidrug Resistant TB and HIV

Multidrug resistant TB is defined when the isolated mycobacteria in a patient is resistant to both isoniazid and rifampicin. See TB guidelines.

Viral Hepatitis/HIV Co-Infection (Principles of Management)

- All HIV-positive persons should be screened for, hepatitis B and C at the time of diagnosis and annually thereafter.

- The following list describes risk factors for acquiring Hepatitis B and C:

- intravenous drugs users, "chem sex"

- presence of mucosal trauma caused by sexual intercourse,
- unprotected anal intercourse,
- history of recent sexually transmitted infections.

Note: Individuals with unexplained increase in liver function tests (LFTs), and a negative anti-HCV antibody test should be screened with a serological test for HCV-RNA. Patients with a positive anti-HBc test, and negative HBsAg with elevated LFTs, should be screened with a HBV-DNA test to rule out occult HBV infection.

- Patient with liver cirrhosis having co-infection with HBV and HBC are at high risk of developing hepatocellular carcinoma (HCC). Individuals with an active HBV infection should be screened at least once a year with a liver ultrasound and/or CT.
- Complications present or evidence of portal hypertension screen and monitor for existing esophageal varices.
- HBV, HCV and HIV, can also be sexually transmitted provide adequate counselling and advice on condom use.
- HIV-positive persons with HBV and/or HCV co-infection may benefit from early ART as it delays liver fibrosis and stimulates the immune response (Viral load suppression).
- ART with a TDF (tenofovir)based regimen is recommended in all persons with HBV (HBsAg-positive) and chronic HCV co-infection irrespective of CD4 cell count.
- Therapeutic management of HIV-positive or negative persons with esophageal varices, hepatorenal syndrome, hepatic encephalopathy or ascites is exactly the same.

HBV vaccination is recommended for the following groups: Annex 9 CDC recommendations

a. Babies and young children
b. Household contacts of people who are HBsAg positive
c. Sexual contacts of HBsAg positive people
d. People on hemodialysis
e. Intravenous drug users
f. Patients with chronic liver disease and/or hepatitis C
g. Inmates and prison personnel
h. Healthcare workers

HIV and Other Infections : Opportunistic Infections (OIs)

OIs are severe infections that occur more frequently in individuals with weakened immune systems, e.g. PLWH. Although basic ART is available in Belize , many individuals still need care for advance HIV disease and OIs. These infections continue to cause important morbidity and mortality in the following groups with further CD4 decline:

1. Patients that are not aware of their HIV infection (late presenters)
2. Patients with poor compliance/adherence to ART (psychosocial, financial factors)
3. Post ART initiation as Immune reconstitution inflammatory syndrome (IRIS).

Prophylaxis against opportunistic infection (OI) is treatment given with specific antibiotics to HIV-infected individuals for the prevention of OIs.

Pneumocystis jirovecii Pneumonia (PCP):

This condition is caused by the yeast-like fungus Pneumocystis jirovecii, and can be seen in those with advanced immunosuppression (CD4 T cells <200/ul).*treat all patients presenting with clinical-radiological findings suggestive of PCP **immediately.**

Table 5: Management of PCP

Opportunistic infection	***prophylaxis***	***Treatment***
Pneumocystis jirovecii pneumonia (PCP)	**Primary Prophylaxis** TMP/SMX (160mg/180mg) tablet po daily or (80mg/400mgSS) tablet po daily Monthly pentamidine inhalations are a well- tolerated alternative. Other options are dapsone and atovaquone. Discontinue CPT after successful immune reconstitution on ART to >200 CD4 T-cells/ll for at least 3 months. **Alternative regimens include**: ❖ Clindamycin: 3–4 x 600 mg i.v. or p.o. + primaquine 30 mg p.o. qd ❖ Pentamidine: 4 mg/kg i.v. 5 days, then reduction if necessary to 2 mg/kg (blood sugar controls must be recorded) ❖ Atovaquone: 750 mg (5 ml) suspension p.o. bid with food	**mild PCP outpatient setting-(ABG's with Pa02 > 80 mm Hg or peripheral saturation > 90mmHg) treat with oral TMP/SMX for 21 days** **For mild–moderate disease** (PaO2 > 70 mm Hg), oral co-trimoxazole 90 mg/kg/day 21 days In mild disease dapsone 100mg po od and trimethoprim 20mg/kg/day po 21/7 or atovaquone 750mg bid po 21 days may be considered **For moderate-severe disease** (PaO2 <70 mm Hg), TMP 15–20 mg per kg/day (SMX 75–100 mg per kg/day) applied in 3–4 daily doses (21 days total) + Prednisone 50-100 (~1 mg/kg/day for 5-10 days **Severe PCP --Must be hospitalized**

Cerebral Toxoplasmosis:

This OI is associated with the reactivation of a latent Toxoplasma gondii infection (an obligate intracellular protozoan parasite). Extra cerebral manifestations of this condition are rare.

Empirical treatment is recommended if lesions suggestive of toxoplasmosis are seen using CT scanning or MRI. Steroids (dexamethasone 4–8 mg/day tid or quid). can be indicated in patients with increased intracranial pressure or extensive brain edema.

Note: Primary cerebral lymphomas also respond to steroids, and in the case of therapeutic failure a biopsy should be considered.

Table 6:Toxoplasma gondii encephalitis (TE)

Opportunistic infection	***prophylaxis***	***Treatment***
Toxoplasma gondii encephalitis (TE)	**Prophylaxis:**Exposure prophylaxis: Immunoglobulin G (IgG) negative patients should avoid eating raw or undercooked meat. No evidence that proximity to cats increases the risk for this condition. **Primary prophylaxis**: IgG positive patients with <100 CD4 cells/ll TMP/SMX (5mg/kg TMP and 25mg/kg SMX). Discontinue **prophylaxis if CD4 cell count is >200 cells/ll for at least 3 months.** **Secondary prophylaxis**: In the absence of immune reconstitution, This maybe a lifelong scenario with half the dose needed for acute therapy.	**<u>Preferred therapy for 6 weeks</u>** Pyrimethamine 200 mg po daily , then 50 mg (<60 kg) to 75 mg (≥60 kg) po daily *plus sulfadiazine 1,000 mg (<60 kg) to 1,500 mg (≥60 kg) po q6h *plus leucovorin 10–25 mg po daily (can increase 50 mg) longer duration if clinical or radiologic disease is extensive or response is incomplete at 6 weeks TMP-SMX (5 mg/kg TMP and 25 mg/kg SMX) IV or po bid; or **<u>chronic maintenance therapy</u>** Pyrimethamine 25–50 mg PO daily + sulfadiazine 2,000–4,000 mg po daily (in two to four divided doses) +leucovorin 10–25 mg po daily *Continue maintenance if there is an immune reconstitution of >200 CD4 cells/ll for at least 3–6 months

C ytomegalovirus (CMV) herpes family:

CMV reactivation is more common in patients with CD4 cell count is < 100 cells/ll, and may present as CMV retinitis, and others including CMV colitis and manifest with**: weight loss,anorexia,abdominal pain and diarrhea, perforation with acute abdomen (clinical management is the same).**

In HIV Patients diagnosed with CMV infection CMV-specific therapy and ART immediately. Extraocular manifestations of (encephalitis, ventriculitis) are treated in the same way. Consider **intravitreous injections during the first trimester of pregnancy.**

Table 7:Management of CMV

Opportunistic infection	***prophylaxis***	***Treatment***
Cytomegalovirus (CMV) disease	**Primary prophylaxis**: CMV retinitis- ganciclovir if CD4 T-cell count of <50 cells/ll *monitor toxicity *Fundoscopy every (3 months) **Secondary prophylaxis-** may be needed with oral ValGCV after ending Acute therapy. Discontinue after 6 months of maintenance therapy or if there is an increase in the level of of CD4 cell count of > 100–150 cells/ ll.	**CMV retinitis;** sight-threatening lesions Ganciclovir intraocular implant + valganciclovir 900 mg po (bid for 14–21 days, then once daily) One dose of intravitreal ganciclovir can be administered immediately after diagnosis until ganciclovir implant can be placed For small peripheral lesions;Valganciclovir 900 mg po bid for 14–21 days, then 900 mg po daily chronic maintenance therapy -for CMV retinitis Valganciclovir 900 mg po daily; or Ganciclovir implant (may be replaced every 6–8 months if CD4 count remains <100 cells/μL) + valganciclovir 900 mg po daily until immune recovery CMV esophagitis or colitis Ganciclovir IV or foscarnet IV for 21–28 days or until resolution of signs and symptoms -PO valganciclovir can be used if tolerated orally Consider maintenance therapy if relapses **CMV pneumonitis:**Treatment should be considered in patients with histologic evidence of CMV pneumonitis, who do not respond to treatment of other pathogens. The role of maintenance therapy has not been established CMV neurological disease- ganciclovir IV + foscarnet IV until symptomatic improvement. Maintenance therapy (with valganciclovir po + IV foscarnet)for life unless immune recovery is evident

Candidiasis

C. albicans being the most frequent agent, and can be part of the normal gastrointestinal flora. Oropharyngeal and vulvovaginal disease are the most common forms seen in persons with immunosuppression. Esophageal candidiasis (thrush) does not require an endoscopy study to confirm diagnosis if typical lesions exist in the mouth; refractory cases have been reported in advanced HIV disease.

Table 8:Candidiasis

Opportunistic infection	***prophylaxis***	***Treatment***
Candidiasis (mucosal	**Basic Prophylaxis includes** *changing toothbrush regularly and thorough cleaning of dentures *HIV-infected children and adults with OC can be treated with chlorhexidine 0.12 % daily for a 3 month period, as a mouth rinse	Cutaneous candidiasis -Clotrimazole If Oral candidiasis-Nystatin 500000 unit 5ml every 6 hrs for 7-14 days-swish and swallow Fluconazole-= 100 -200 mg daily for 5–14 days). **Esophageal candidiasis** – Fluconazol 200–400 mg daily for 10–14 days. Patients with severe dysphagia can initially be treated intravenously and switched to oral as symptoms improve. If fluconazole resistance has been detected, use (itraconazole, voriconazole and posaconazole) before parenteral therapy is initiated (e.g., with echinocandin). ART should be initiated immediately if chronic recurring

Herpes simplex infections (HSV)

HSV is a double stranded DNA virus. There are two types:Type 1 (HSV-1) and Type 2 (HSV-2). Infections with HSV can be atypical in patients with severe immunosuppression and is categorized as an AIDS-defining illness.

Table 9: Herpes simplex infections (HSV)

Opportunistic infection	***prophylaxis***	***Treatment***
Herpes simplex virus (HSV) disease HSV-1 and HSV-2	**Primary prophylaxis is not recommended.** **Long-term treatment** -acyclovir (400–800 mg bid or tid) Or ValACV (500 mg bid) can still be effective treatment for recurrent HSV (at least 6 months). Encourage use of latex male/female condoms	**Topical treatment** with acyclovir for discrete oral lesions. **Systemic treatment+ organ involvement:** IV acyclovir. **Encephalitis**:Acyclovir (400 mg 3-5 times a day p.o. , severe cases 10 mg/kg i.v 3-5 times a day or 800 mg 5 times a day p.o. or Valacyclovir 1,000 mg 2-3 times a day Uncomplicated genital herpes famcyclovir 500 mg for 2 days.

Varicella Zoster Infection (VZV)

Varicella zoster virus infection may present as an acute infection (chicken pox) and as a reactivation (zoster/shingles). Acute infection is less common due to the availability of vaccination but may present with more severe symptoms in PLWH. Other presentations of VZV infections could be pneumonia, encephalitis, ophthalmic zoster**.**

Table 10: Varicella Zoster infection (VZV)

Opportunistic infection	***prophylaxis***	***Treatment***
Varicella zoster virus (VZV) disease		Uncomplicated Herpes Zoster = Acyclovir 800 mg 5 x/ daily p.o. for 7 days or Valacyclovir 1,000 mg 3/daily x p.o. x 7-10 days Famcyclovir and ValACV are alternatives. Severe/Complicated HZ (multisegmental or facial zoster) Acyclovir (10–15 mg/kg IV tid for 10-14 days). After clinical improvement is evident, a switch to oral therapy is possible.

Table 12: Nontuberculous Mycobacteria (NTM):

Opportunistic infection	***prophylaxis***	***Treatment***
Nontuberculous Mycobacteria (NTM):MAC complex	NTM diseases, can be seen in patients with CD4 cells <50. Mycobacterium avium complex or M. intracellular (Mycobacterium avium intracellular complex, MAI) other Pulmonary NTM are . kansasii, xenopi,malmoense, and M. abscessus.	**<u>Treatment:</u>** A combination treatment of a macrolide (clarithromycin or azithromycin) and ethambutol plus/minus rifabutin is recommended. Rifabutin is preferred to rifampicin due to its in vitro efficacy against MAI and its lower interaction potential. Clarithromycin 500 mg bid or Azithromycin (1200 mgs orally once weekly or 600 mgs orally twice weekly) Plus ethambutol 15 mg/kg PO daily for 12 months. If asymptomatic stop treatment after 1 year and with CD4 >100 mm^3 for at lest 6 months ART can be delayed after the 2 wks due to IRIS and pill burden.

Cryptosporidiosis

This infection is caused by Cryptosporidium parvum after feco-oral contamination. In some cases this condition may involve the biliary tract, leading to sclerosing cholangitis

Opportunistic infection	*prophylaxis*	*Treatment*
Cryptosporidiosis	**There is no accepted prophylaxis for this condition.** This presents as chronic diarrhea in HIV positive persons with CD4 T-cell counts of <100cells/l	Successful ART may lead to complete resolution of this condition. Symptomatic treatment -loperamide (2 mg p.o bid or quid) and/or tincture of opium 1 % at 5–15 drops quid) Nitazoxanide can be an alternative (500–1000 mg PO BID with food for 14 days)

Microsporidiasis

Microsporidia are a group of obligate intracellular parasitic fungi causing zoonotic and/or waterborne disease, mostly causing diarrhea in PLWH. Other manifestations of microsporidiosis are: encephalitis, ocular infection, sinusitis, myositis, genitourinary, and disseminated infection.

Opportunistic infection	*prophylaxis*	*Treatment*
Microsporidiasis	**<u>WASH</u>** **<u>Diagnosis:</u>** identification of microsporidia in the stool using light microscopy. Biopsy of small bowel	**<u>Treatment:</u>** Initiate ART as soon as possible in combination with fluid therapy and other drugs. Albendazole (400 mgs orally bid until immune reconstitution has been maintained for 6 months).

Cryptococcal Infection:

Cryptoccocosis is a disease caused by Cryptococcus neoformans an encapsulated yeast and is one of the most common OI's in PLWH and CD4 cell count is <200 cells. Some serotypes can be found in the pigeon feces, not causing disease in them.Transmission occurs via inhalation of infected particles resulting in with pulmonary symptoms. In PLWH with severe immunodeficiency this condition usually involves the CNS causing meningitis.

Table 11:Cryptococcal Infection

Opportunistic infection	*prophylaxis*	*Treatment*
Cryptococcal meningitis	**Prophylaxis-**There is no clear survival benefit in primary prophylaxis. Secondary prophylaxis can be discontinued after at least 6 months maintenance therapy and a CD4 of >100 cells/ll and undetectable VL within 6 months	**<u>Recommended induction therapy</u>** Amphotericin B deoxycholate (AmB-D) 0.7–1.0 mg/kg/day i.v. and flucytosine (100 mg/kg/day i.v. or p.o. if available), divided into four doses a day. Acute therapy-duration is 14 days. Then fluconazole (400 mg/day) for 8 weeks. Optional in countries with limited resources. fluconazole as initial daily dosages of 800–2,000 mg. *measure intracranial pressure at diagnosis. If the intracranial pressure is very high, do Lumber punctur until it is < 20 cm. **cryptococcal pneumonia** (negative CSF diagnosis), Fluconazole (400 mg/day) for 6–12 month.

Histoplasmosis:

Fungal disease caused by Histoplasma capsulatum. This fungus is found in soils with high nitrogen content as the ones enriched with bird or bat guano. Environmental exposures during (cave exploration,wood cutting, excavation of sites) increase the risk for this infection. Factors associated to histoplasmosis are CD4 levels <200/mm^3, and the abscense of ARV. Histoplasmosis is usually asymptomatic and self limiting,but in PLWH,with presentation from latent to fulminant forms (septic shock, multi-organ involvement). non-specific symptoms include : fever, fatigue weight loss, respiratory symptoms, hepatosplenomegaly and superficial adenopathy.

Table 12:Histoplasmosis

Opportunistic infection	***prophylaxis***	***Treatment***
Histoplasma capsulatum infections		**Moderately severetosevere disseminated disease** **Induction therapy** (for 2 weeks or until clinically improved) Amphotericin B at 3 mg/kg IV daily **Maintenance therapy** Itraconazole 200 mg PO tid for 3 days, then bid to complete 2 weeks **Preferred therapy for less severe disseminated disease** Induction and maintenance therapy Itraconazole 200 mg PO tid for 3 days, then 200 mg PO bid x 12 months **Preferred therapy for meningitis** **Induction-**(4–6 weeks) Liposomal amphotericin B 5 mg/kg/day **Maintenance therapy** Itraconazole 200 mg po bid for ≥1 year and until resolution of abnormal CSF findings **Preferred therapy for long term suppression therapy** Itraconazole 200 mg PO daily until achieving immune reconstitution.

Syphilis:

Is an infectious veneral disease cause by Treponema pallidum, manifestations of syphilis in PLWH are identical to those seen in HIV negative persons. Syphillis is classified into 4 stages: primary, secondary, latent and tertiary.
Primary syphilis usually presents as a single painless nodule at the site of contact that rapidly ulcerates to form a classic chancre.
Secondary syphilis may appear 2 to 8 weeks after primary inoculation. Manifestations include macular, maculopapular, pustular mucocutaneous lesions of the palm and soles, generalized lymphadenopathy, fever, malaise, anorexia, arthralgias, and headache.
Other clinical presentations include: hepatitis, nephrotic syndrome, gastritis, pneumonia. These manifestations may persist from a few days to weeks before resolving and/or progressing to a latent state.
Latent syphilis is characterized by a positive serological reaction with no clinical signs or symptoms of the infection.

Tertiary syphilis: Clinical manifestations of this advanced stage (Neurosyphilis) are:

- cranial nerve dysfunction
- auditory or ophthalmic abnormalities
- meningitis
- stroke,
- acute or chronic mental alterations
- gummous syphilis

Other manifestations include ophthalmic and cardiovascular syphilis.

Definitive Diagnosis: Darkfield microscopy and tests to detect *T. pallidum* in lesion exudates (e.g., DFA-TP) or tissue (e.g., biopsy with silver stain) for early syphilis.

Diagnosis of neurosyphilis: Uses a combination of laboratory findings in the CSF (cell count, protein, and a CSF-VDRL) and clinical evidence. Findings in the CSF may include:

1. mononuclear pleocytosis (6–200 cells/mm^3)
2. mildly elevated protein concentration
3. reactive CSF- VDRL

Screening:

- Yearly screening for in HIV positive persons who are sexually active, and every 3–6 months for those who have multiple or anonymous partners.
- All individuals who had sexual contact with a person diagnosed with syphilis.
- If serologic tests are negative, no treatment is needed,
- If positive, treatment should be based on clinical staging and serologic evaluation
- Long- term sex partners of persons diagnosed with latent syphilis should be clinically and serologically evaluated and treated according to findings.

Managing treatment Failure or Reinfection - following group of patients:

1. Patients with early-stage syphilis, or with persistent/recurring clinical signs or symptoms
2. Patients with sustained four-fold increase in titers after an initial reduction following treatment.

Syphilis during Pregnancy:

1. All pregnant women must be screened for syphilis at the first prenatal visit/evaluation, at 28–32 weeks of gestation and at delivery.
2. All mothers and neonates should not leave the hospital without documentation of their serologic status
3. All women with a fetal death after 20 weeks of gestation, must have a serologic test for syphilis.
4. Penicillin is the only known effective antimicrobial for preventing maternal transmission to the fetus and for treatment of fetal infection.

Opportunistic infection	*prophylaxis*	*Treatment stages*
Treponema pallidum infection (syphilis)		Early Stage (Primary, Secondary, and Early-Latent Syphilis) • Benzathinic penicillin G 2.4 million U IM single dose Penicillin-Allergic Patients): **Doxycycline 100 mg po BID for 14 days , or Ceftriaxone 1 g IM or IV daily for 10–14 days.** **Pregnant women with early syphilis**, a second dose of Benzathinic penicillin G 2.4 million units IM after one week of the single dose treatment may be considered. Late-Latent (>1 year) or of Unknown Duration : Benzathinic penicillin G 2.4 million U IM weekly for 3 doses. ❖ Doxycycline 100 mg po BID for 28 days Note: Persons with penicillin allergy whose compliance or follow-up cannot be ensured should be desensitized and treated with ❖ Benzathinic penicillin **Late-Stage** (Tertiary—Cardiovascular or Gummatous Disease-Neurosyphilis, Otic, or Ocular Disease ❖ Crystalline penicillin G, 18–24 million U per day, administered as 3–4 million U IV q4h or by continuous IV infusion for 10–14 days +/- Benzathinic penicillin G 2.4 million U IM weekly for 1 to 3 doses after completion of IV therapy ❖ **Alternative Therapy:** ❖ Procaine penicillin G 2.4 million U IM daily + probenecid 500 mg po QID for 10–14 days (BII) +/- Benzathinic penicillin G 2.4

		million U IM weekly x 3wks after completion of above ❖ Allergic to sulpher-containing medications do not use probenecid ❖ Allergic Patients to penicillin ceftriaxone 2 g IM or IV daily for 10–14 days

Progressive Multifocal Leukoencephalopathy (PML):

PML is a severe demyelinating disease of the brain (CNS) associated with the John Cunningham virus (JCV). Asymptomatic primary JCV infection is seen in children and is followed by a chronic asymptomatic carrier state that can only detected by the presence of viral DNA in the urine. **ART produces a reduction in the disease progression and remission but not a reduction in mortality**

PML is a rare and fatal disease with episodes of spontaneous remissions and is **characterized by**:

5. being of insidious onset in nature
6. focal and progressive neurological deficits, due to multiple scattered demyelinating lesions in the brain.
7. rare spinal cord involvement.
8. the prescence of partial deficits (e.g., weakness in one leg) that worsen over time as larger territories of white matter are involved (hemiparesis).

The focal or multifocal nature of this disease is responsible for the distinct clinical presentations (diffuse encephalopathy, isolated dementia or as a behavioral syndrome). The demyelination evolves with clinical progression over several weeks, this helps to differentiate PML from other focal brain disorders.

PML may present also with: headache, fever and seizures as a result of lesions immediately adjacent to the cortex. Diagnosis is based on a combination of clinical and neuroimaging studies (Magnetic resonance imaging (MRI), and the use of JVC DNA-PCR in CSF)

Human Papillomavirus Disease (HPV)

Infection with HPV is a major risk factor for development of cervical cancer in women. Cervical infection with HPV is common and occurs primarily through sexual transmission. Penetrative sexual intercourse is not necessary for HPV transmission. Persistent oncogenic HPV infection with HPV 16 and 18 is needed for the development of cervical cancer. Types 6 and 11 are associated with genital warts, and are not considered oncogenic. HPV related cancers include those located in the anus, vulva, vagina, penis, oral cavity, and oropharynx.

Diagnosis of genital and oral warts is by clinical evaluation and must be confirmed by biopsy. The same Exfoliative cytology test (Pap test), and colposcopy with biopsy detect CIN among HIV- seronegative and seropositive patients.

Table 13:Humanpapillomavirus disease

Opportunistic infection	***Prophylaxis***	***Treatment***
Human papillomavirus disease	Vaccination with commercially available HPV vaccine **is not recommended** during pregnancy **/prevention** 1. HPV vaccines are recommended to prevent this condition and they should be administered before any sexual exposure to HPV 2.The use of latex condoms will lower the incidence of transmission of HPV, HIV infection and STIs. 3. Male circumcision may reduce the rates of HPV infection	**unmplicated external warts** Imiquimod (5% cream) apply at bedtime 3 x weekly x 16 weeks, until lesions are no longer visible. The treatment area should be washed with soap and water 6 to 10 hours after the application Podofilox 0.5% solution or gel applied to visible anogenital warts 2 x a day for 3 days, followed by 4 days of no therapy. Repeat cycle four times. *Cryotherapy, trichloroacetic acid (TCA), bichloroacetic acid (BCA), and surgery, are typically recommended for complex or multicentric lesions Oral warts = no optimal treatment, surgery may be necessary. For persistent or recurrent genital warts retreatment may be necessary with any of the drugs previously described. Biopsy should be considered to exclude VIN. Genital warts often require more than one course of treatment. Podofilox should not be used during pregnancy.Pregnancy-Ablative therapies (i.e., laser, cryotherapy, and excision) can be used during pregnancy.

Opportunistic infection	*prophylaxis*	*Treatment*
Leishmaniasis, cutaneous		Acute infection: Amphotericin B 2–4 mg/kg IV daily for 10 days or interrupted schedule (e.g., 4 mg/kg on days 1–5, 10, 17, 24, 31, 38) to achieve total dose of 20–60 mg/kg; or Sodium stibogluconate 2mg/kg IV or IM daily for 3–4 weeks

Initiating ART Following Acute Opportunistic Infections Recommendations:

1. Consultation with a clinician with experience in management of ART in the setting of acute OIs is recommended
2. Clinicians should start treatment for acute opportunistic infections (OIs) and evaluate initiating ART within 2 weeks
3. In patients with tuberculous meningitis or cryptococcal meningitis sart ART immediately.
4. In persons with TB/HIV coinfection initiate ART within 2 to 8 weeks of starting TB treatment. See TB guidelines.

Helping HIV-infected Patients to Avoid Exposure or Infection from Opportunistic Pathogens

Pet Related Exposures

1. In general, the probability of acquiring infections can be reduced by practicing proper hygiene (hand washing)
2. Contact with stool from pets or stray animals should be avoided.
3. Limit contact with or avoid reptiles, chickens and ducklings because of the high risk for exposure to *Salmonella spp*. Also limit contact with cats to avoid Toxoplasmosis.
4. Gloves should be used during aquarium cleaning to reduce the risk of infection with *Mycobacterium marinum*.
5. Contact with exotic pets (e.g., nonhuman primates) should be avoided.

Water and Food

1. PLWH must not drink tap water and water from pools, lakes or rivers.
2. PLWH should avoid swimming in water that is contaminated with human or animal waste.
3. PLWH should use bottled or boiled water to eliminate the risk of acquiring viral, bacterial, and other parasitic infections..
4. PLWH, should not consume the following: raw or undercooked eggs, raw or undercooked meat, seafood, shellfish, unpasteurized dairy products (including milk and cheese), and fruit juices.
5. Microwave cooking is not recommended

Immune Reconstitution Syndrome (IRIS):

Definition: A paradoxical clinical worsening of a known condition or the appearance of a new condition after initiating ART resulting from restored immunity to specific infectious or non-infectious antigens. No test is available to confirm IRIS diagnosis. Current theories to explain etiology are:

- Underlying antigenic burden
- Degree of immune restoration following ART
- Host genetic susceptibility

Major Criteria:

1. Atypical presentation of OI's or tumors
2. Reduction in plasma HIV RNA level by at least 1 log10copies/mL
3. History of OI's

Minor Criteria:

1. The presence of an increase CD4 cell count after ART
2. Increase in immune response specific to a specific pathogen
3. Spontaneous resolution of disease without specific antimicrobial therapy or tumor chemotherapy with continuation of ART

Risk Factors:

a. Male sex
b. Younger age
c. Lower CD4 level at ART initiation
d. Higher HIV RNA at ART initiation
e. Lower CD4 level percentage at ART initiation
f. Lower CD4/CD8 ratio at ART initiation
g. Rapid initial fall in HIV RNA on ART
h. Antiretroviral naïve at time of OI diagnosis
i. Shorter interval between OI therapy initiation and ART initiation

Note: IRIS does not appear in all patients taking ART, but may be more frequent in those with a low CD4 T-cell count of <50 cells/ll

Treatment:

Steroid therapy for 2–6 weeks is recommended the use of non-steroidal anti-inflammatory drugs (NSAIDs) may be use in mild to moderate cases. ART should only be interrupted in very severe cases.

HIV and Other Non-Infectious Co-morbidities

Adipose Tissue Dysfunction and HIV/AIDS

Adipose tissue dysfunction and altered fat metabolism contribute to the development of chronic disease. Lipoatrophy and lipohypertrophy mayybe associated to ART. These adipose tissue abnormalities (lipodystrophy), have increased fibrosis without inflammation, increased small adipocyte numbers and decreased vascularity.

Alternatives for the prevention and treatment of adipose tissue dysfunction:

Prevention strategies for lipoatrophy	**Management**
1. Avoid ZDV containing regimens. 2. Avoid excessive weight loss due to diet and exercise.	1. Modification of ART 2. Switch to regimen not including NRTIs for example, ABC or TDF: 3. Only ART modification proven to partially restore subcutaneous fat; 4. Surgical intervention— Offered for cosmetic relief of facial lipoatrophy only
prevention for lipohyperthrophy	**Management**
1. There is no proven strategy 2. No current antiretroviral drug has been clearly associated with increased visceral adiposity 3. An excess of visceral fat has been reported in HIV vs. non-HIV non-obese persons for the same body mass index 4. Weight reduction or avoidance of weight gain may decrease visceral fat 5. Avoid inhaled fluticasone (and potentially other inhaled corticosteroids) with RTV as it may cause Cushing syndrome or adrenal insufficiency	1. Diet and exercise 2. Diet and exercise are needed to maintain reduction in visceral fat **3.** Pharmacological interventions to treat lipohypertrophy have not been proven to give long-term effects and may introduce new complications

Dyslipidemia and HIV

Hyperlipidemia can be seen in HIV-infected patients as a result of or maybe aggravated by the use of ART. Statins undergo different levels of metabolism via one or more of the cytochrome P450 isozymes of the liver or gastrointestinal tract. **General principles in the treatment of Dyslipidemias**

1. Higher LDL-c levels increase risk of CVD, consequently its reduction decreases this risk; the reverse is probably true for HDL-c.
2. The CVD risk implications from higher than normal TG levels are not clear, as TG has not consistently been shown to independently predict the risk of CVD.
3. Less calories, more exercise, reducing bodyweight, and stop smoking tend to improve HDL levels. Eating fish, reducing caloric intake, and minimizing the intake of saturated fat and alcohol will help to reduce triglyceride levels.
4. Statins should be used by all those with established vascular disease and among those with type 2 diabetes or at high risk of CVD, regardless of lipid levels.

NNRTI inhibitors and Statins

drugs	Enzyme acted upon	Time of effect	effect
Nevirapine (Viramune) efavirenz (Sustiva-600mg)	CYP3A4	Time 24 hours	reduces
Protease Inhibitors and Statins: ritonavir (Norvir)-and PI combinations.		Time 24 hours	reduces
Integrase inhibitors has no effect on statin plasma levels.			No effect

Manifestations of Statin Toxicity/adverse effects are:

- Skeletal muscle injury (myalgia, acute myositis)
- Myopathy (increased levels of creatine kinase (CK), lactate dehydrogenase, and transaminases.
- Rhabdomyolysis
- Acute renal failure
- Severe electrolyte imbalances.
- Hepatic dysfunction

Glucose Abnormalities and HIV

ART such as (NRTI's and PIs) may alter blood glucose levels in PLWH as a result of abnormalities in the glucose and insulin metabolism .

Treatment goals in diabetes management in PLWH are:

1. Prevention of hyper/hypoglycemia, glucose control (HbA1c < 6.5% without hypoglycemia, maintain fasting plasma glucose 4-6 mmol/L (73-110 mg/dL), to prevent long-term complications
2. To achieve normal blood lipids, and blood pressure < 130/80 mmHg,
3. Acetylsalicylic acid (75-150 mg qd) must be considered in diabetics with elevated underlying CVD risk
4. Nephropathy, polyneuropathy and retinopathy screening should be performed as in diabetic persons without HIV

Metformin: Improves endothelial function and does not affect lipid profiles, but it may worsen lipoatrophy. Start dose (500-850 mg qd), increase to max tolerated dose of (2-3) g/day over 4-6 weeks.

PIs increase plasma concentration of oral hypoglycemic agents such as sulfonylurea, glitazones and meglitinides, while NNRTI's cause a reduction. Insulin use is safe in patients with HIV due to lack of ART interactions, its acceptability in renal and hepatic dysfunction, due to its anabolic and anti-inflammatory effects.

Cardiovascular Risk in HIV/AIDS

HIV increases the risk of heart disease in adults and children.The reason for this is multifactorial:

1. High prevalence of traditional cardiovascular disease risk factors
2. Genetic factors
3. Possible direct HIV effects, and the sequeale of chronic inflammation related to HIV infection (increased concentrations of C reactive protein, interleukin 6 and d–dimer has been associated with cardiovascular disease in patients with HIV). ARVs such as EFV increases total and LDL cholesterol concentrations a bit more when compared to PI's.

Providing Care for the Patient with Advance HIV Disease

Definition : Advance disease in adults and adolescents and children more than 5 years old is defined when the CD4 cell level is less than 200 cells/m^3. All children < than 5 years old with HIV are considered to have advance disease.

Patients with advanced HIV disease must be carefully assessed keeping in mind the CD4 cell level/ VL and the WHO clinical staging: look for the following.

1. Is the patient seriously ill? Does the patient need to be admitted?
2. Is the patient compliant or adhering to medication or receiving ART that is failing?
3. Are there any signs and symptoms suggestive of tuberculosis or is the patient receiving treatment for tuberculosis?
4. Is the patient diagnosed with or has signs or symptoms of the following conditions Cryptococcal meningitis, cerebral toxoplasmosis, severe PCP, CMV or fungal infections?
5. Diagnostic tests to consider: VL to evaluate for possible treatment failure, sputum Xpert MTB/RIF, CD4 cell levels, to consider lumbar puncture, x rays and cultures.
6. Once diagnosis is confirmed starting treatment is a priority
7. If access to investigations is limited or there are delays to obtain results presumptive treatment must be initiated and ART should not be delayed.

HIV and the Elderly

ART therapy has incidence and prevalence of HIV in the elderly producing and positive impact by increasing the survival rates of HIV positive person. Areas of concern in the elderly HIV patients are:

A. Older PLWH may suffer from aging related comorbid illness.
B. HIV infection may affect the biology of aging (early association of clinical syndromes associated to advance age).
C. Reduction in immunological and mucosal defenses and changes in risk related behaviors in this population could lead to increase risk acquisition and transmission of HIV. (e.g. reduction in condom use because of less concern about pregnancy or more high risk sexual activity with increase use of erectile dysfunction drugs)
D. Older individuals are generally perceived to be at low risk for HIV infection, and screening for this population remains low.

Diagnosis and Prevention: Test and educate all persons older than 50 years for HIV.

ART in the Older Individual

Early treatment is needed in older adults as a result a reduction in the immune recovery and an increased risk of other comorbid diseases not related to HIV. ART treatment must consider existing medical conditions, drug to drug interactions, response to ART and timing of multiple medications and a reduction in liver and kidney function that can impair elimination and drug exposure.
Clinicians should expect that clinical response or immune improvement or CD4 cell recovery in older patients will be in general slower when compared to younger patients.

Poor compliance to ART is therefore the main cause of treatment failure. Other causes are complex dosing requirements, high pill burden, lack of access to medications, high cost and availability, literacy issues that can cause misunderstanding of instructions, depression, and neurocognitive impairment.

HIV and Adolescents

Adolescence is defined as the period between ages 10 to 19 years, and it is here that individuals undergo physical, psychological and sexual changes or maturation. These changes affect the provision of appropriate treatment and care for HIV-infected adolescents. ART see table 5

Considerations and Challenges in HIV positive Adolescents

Dosing: Based on the choice of ART regimen, the dosages for adolescents should be based on sexual maturity rating (i.e. Tanner staging) www.mtnstopshiv.org/sites/default/files/attachments/TannerStaging2.pdf

Adherence to ARV in Adolescents

Adherence to long-term therapy difficult among adolescents: the following factors must be considered to achieve optimal adherence to ART:

- Perception by adolescents of being immortal
- Desire for independence
- Lack of disclosure of HIV status due to fear of stigma and discrimination
- Non-disclosure by parents to HIV infected child due to fear of stigma or blame from their children.

Education and information is important for adolescents to progress completely through the transition process into adult care. HIV-infected adolescents are vulnerable and may develop adherence problems as a result of psychosocial and cognitive development issues. A comprehensive system of care should assess ways to cope with the following:

- Denial and fear of their HIV infection
- Misinformation
- Distrust of the medical establishment
- Fear and lack of belief in the effectiveness of medications
- Low self-esteem
- Unstructured and chaotic lifestyles
- Mood disorders and other mental illness
- Lack of familial and social support
- Absence of or inconsistent access to care
- Disclosure of HIV status if this has not been done by their parents
- Developmental delay
- The transition from pediatrics to adult care, including the choice of appropriate ART regimens
- Physical and psychological changes associated with adolescence that have implications for the provision of appropriate HIV treatment and care.

Transitioning from Pediatric HIV Care

An adolescent who is moving from pediatric HIV care to adult care requires management and support by parents, guardians and health professionals. In many instances adolescents require a more "teen-centered" and multidisciplinary approach

For successful transitioning consider the following:

- Optimizing provider communication skills
- Addressing patient/family resistance caused by lack of information, stigma or disclosure concerns, and differences in practice styles
- Preparing young patients for life through the development of skills that must include, counseling on the appropriate use of the health services, the importance of a fast and accurate recognition of symptoms with a dependable reporting to the clinician, and to emphasize the importance of self-care and medication compliance
- Antiretroviral therapy regimens must be individually tailored to the adolescent
- Patients and health care providers must engage in regular multidisciplinary case assessments , including adult/adolescent and pediatric care providers
- Implementation of interventions that may be associated with improved outcomes, such as support groups and mental health consultations
- Regular discussions on reproductive health (preconception care and contraceptive methods, safe sex , HIV and STI prevention) should be held
- All adolescents should be receiving maximally suppressive antiretroviral therapy
- Providers should be aware of potential interactions between antiretroviral therapy and hormonal contraceptives that could lower contraceptive efficacy

Pre-Exposure Prophylaxis (PrEP) in HIV

ARVs as prophylactic therapy has been shown to reduce HIV transmission in men who have sex with men (MSM), HIV-discordant couples, injection drug users (IDU) and heterosexual men and women. This strategy involves the daily use of a fixed-dose combination of tenofovir (TDF) and emtricitabine (FTC) with repeated condom provision, sexual risk-reduction counseling, and the diagnosis and treatment of sexually transmitted infection (STI). **The recommendations for the use of PrEP, should be done on a strict individualized basis which includes (proper reporting, status disclosure by the persons involved, documented risk assessment and commitment to adherence.) These drugs are costly and would pose extra economic burden to the country if not indicated and applied properly.**

Recommendations for Pre-exposure Prophylaxis are as follows:

1. Daily oral PrEP with the fixed-dose combination of Trovada (tenofovir (TDF) 300 mg and emtricitabine (FTC) 200 mg) is recommended for adults.
2. For MSM with high risk sexual behavior PrEp may be used "on demand" (double dose of TDF/FTC, 2-24 hours before each sexual intercourse, followed by two single doses of TDF/FTC, 24 and 48 hours after the first drug intake. If dose "on demand" the total dose per week should not exceed 7 tablets).
3. Individuals using PrEP need to be informed that five to seven days of therapy are needed before achieving full protection for anal intercourse and 20 or more days for vaginal intercourse.

A first step for PrEP is to do an assessment of sexual practices and risk behavior:

- Alcohol abuse and other illicit non-injection drugs
- Sexual patterns and practices
- Compliance with medication
- History of bacterial STIs within the past 6 months

Clinicians must clearly educate and discuss with each patient the different types of prevention methods. **Note: PrEP does not protect against other STI except HIV.**

Laboratory Testing to be performed:

1. HIV testing must be performed before starting therapy and every 3 months before prescriptions are refilled .
2. Screen for hepatitis B virus infection (HBV) and evaluate kidney function before starting treatment.
3. Patients with Chronic Renal failure (HIV negative) with an estimated creatinine clearance (eCrCl) of <60 ml/min, should not use PrEP

Summary:

- PrEP is only effective when used as indicated.
- The most important way to have compliance for this therapy is to offer PrEP as a choice.
- PrEP can be discontinued 28 days after the last potential exposure to HIV infected fluids if the person is no longer at risk.

Table 14:Recommendations

Recommendations for PrEP by MSM :
A. Adult man
B. Individual without acute or established HIV infection
C. Any male sex partners in past 6 months (if also has sex with women)
D. Not in a monogamous partnership with a recently tested, HIV-negative man
And at least one of the following :
E. Any anal sex without condoms (receptive or insertive) in past 6 months
F. Any STI diagnosed or reported in past 6 months
G. Is the person is in an ongoing sexual relationship with an HIV-positive male partner
RECOMMENDED INDICATIONS FOR PREP USE BY HETEROSEXUALLY ACTIVE MEN AND WOMEN
A. Adult person
B. Individual without acute or established HIV infection
C. Any sex with opposite sex partners in past 6 months
D. Not in a monogamous partnership with a recently tested HIV-negative partner
And at least one of the following:
E. Is a man who has sex with both women and men (behaviorally bisexual)
F. Infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be at substantial risk of HIV infection (IDU or bisexual male partner)
G. Is in an ongoing sexual relationship with an HIV-positive partner

Post-exposure Prophylaxis (PEP) In HIV

PEP is the use of ARV's for protection and prevention by a person at risk of acquiring HIV infection. PEP must be initiated within 72 hours of exposure.

Assessment of the Risk of HIV Transmission: Factors to be considered are:

- The nature of the exposure
- The risk status of the source
- Factors associated with the source and exposed individual

HIV Transmission Risk/exposure : Being for condomless sexual contact, similarly when a condom fails.

Factors that modify the risk of HIV transmission

1. The higher the Viral Load (VL) in the source patient, the higher the risk of transmission
2. A sexually transmissible disease (STD) in the source or exposed individual (eg. genital ulcer disease and symptomatic gonococcal infection) can increase the risk of transmission/acquisition.
3. Increased risk is associated if the source ejaculates during receptive anal or vaginal intercourse.
4. The presence of a break in the mucosal integrity, increases the risk of transmission (e.g. trauma, genital piercing or genital tract infection)
5. Penetrating, or percutaneous injuries with a hollow bore needle, direct intravenous or intra-arterial injection with a needle or syringe containing HIV infected blood will also increase the risk of transmission
6. The uncircumcised status of the insertive HIV negative partner practicing anal or vaginal intercourse increases transmission risk.

HIV Status of the Source:

It is imperative to contact the source and after obtaining proper verbal and written consent, an HIV test must be performed as soon as possible.

The following steps must be taken into consideration if the source is available:

- If he or she discloses that they are positive, a verbal and written consent must be obtained before to start treatment (check if the person is on treatment, is compliant, and review CD4 and Viral load levels).
- PEP is not required if the person is taking PreP.
- If the HIV status of the source person is not known or not disclosed, assume that the source is HIV positive.

HIV Status of the Exposed individual:The determination of HIV status of the exposed individual should not be delay the use of PEP. Clinicians must ensure that a baseline HIV test is done and that consent forms for acceptance or refusal are obtained.

When to Start PEP	1. Starting PEP within the first 2 hours of exposure, no later than 48-72 hours 2. duration is 4 weeks 3. re-evaluate all persons on PEP at 48-72 hours for tolerability 4. evaluate discontinuing treatment on an individualized basis if severe side effects

If the source person is HIV positive with undetectable HIV-VL levels, PEP is not be recommended. **A pregnancy test must be performed in all female patients**.

If the source person is HCV positive, liver transaminases, HCV-PCR and HCV serology must be performed after 1 month. **See Table 2**

Table 15: PEP recommendations:

Risk	**Nature of Exposure**	**Status of source person**
Blood	Subcutaneous or Intramuscular penetration with iv or im needle, or intravascular device	HIV positive or recent serostatus unknown but presence of IV risk factors
	Contact >15 min of Mucous membrane or non Intact skin	
Genital Secretions	Anal or vaginal sex	Viremia HIV positive or serostatus unknown but presence of HIV riskfactors. If source person is on ART, PEP should be started, HIV-VL should be repeated, and if undetectable, PEP can be stopped
	Receptive oral sex with Ejaculation	Viremia HIV positive
Intravenous Drug use	Exchange of syringe, needle, preparation material or any other material	HIV positive

Ages	Recommended drugs regimen	Prescribing practices:
Adults and Adolecents	**Lamivudine 150mgs + Zidovudine 300mgs twice daily (Combivir)** **OR** **Tenofovir TDF (300 mgs) + Emtricitabine FTC 200mgs daily (Truvada)** **Plus** **Lopinavir/ritonavir (LPV/r) 400/100 mgs twice daily (Kaletra)**	❖ A full 28-day prescription of ARV should be provided. ❖ Counseling and education are primordial for all individuals initiating HIV PEP.
Children less than 10 years:	zidovudine + lamivudine (ZDV + 3TC) Or ABC'+ 3TC or TDF + 3TC or TDF+FTC Lopinavir/ritonavir (LPV/r) is recommended as the preferred third drug for HIV PEP in children less than 10 years	❖ A full 28-day prescription of ARV should be provided. ❖ Counseling and education are primordial for all individuals initiating HIV PEP.

Immediate Management of and Individual with known or suspected exposure to HIV

1. Do not douche the vagina or rectum after sexual exposure.

2. After oral exposure, spit out blood/body fluids and rinse mouth with water.

3. Wash wounds and skin sites that have been in contact with blood or body fluids with soap and water.

4. Irrigate mucous membranes and eyes (remove contact lenses) with water or saline.

5. Do not use antiseptics or disinfectants into wounds.

Individuals at risk of HIV acquisition who decline PEP must be educated and informed about risk reduction (including PreP) and HIV seroconversion, the person also will need to sign a refusal document .

All patients having PEP should be assessed for renal impairment and ART dosages should be adjusted accordingly. Tenofovir should not be used if creatinine clearance is less than 60mL/min.

HIV Prophylaxis for Victims of Sexual Assault

Victims of sexual assault should be treated in an appropriate healthcare setting and evaluated by the physician on call/duty. Infrequent, cases of HIV transmission following sexual assault has been described.

The assessment has to take into consideration the following:

- Whether or not a significant exposure has occurred
- Assessment and evaluation of HIV status of the alleged assailant
- Whether the victim is ready and willing to accept and complete the PEP regimen
- Also need to consider HIV disease seroprevalence in the area.

However the decision to recommend treatment must rely on the first three factors.

Significant Exposure:

1. Direct contact of the vagina, penis, anus, or mouth with the semen, vaginal fluids, or blood of the alleged assailant, with or without physical injury, tissue damage, or presence of blood at the site of the assault.
2. PEP should also be offered in cases when broken skin or mucous membranes of the victim have been in contact with blood, semen, or vaginal fluids from the alleged assailant. Similarly, PEP should be offered in cases of bites that result in visible blood
3. The absence of visible trauma does not indicate that an assault never happened; microabrasions and bruising are common and the manifestation of these type of injuries following sexual assault may be delayed.
4. PEP should be promptly initiated and not delayed- (do not await for test results from the alleged assailant).
5. If the alleged assailant is HIV-infected, the use of PEP should take into consideration the nature of the exposure and the victim's ability to complete the regimen.
6. If PEP has been initiated and the HIV screening tests of the alleged assailant are found to be negative, (rapid test with third- or fourth-generation EIA or HIV RNA assay, PEP should be discontinued after consultation with a clinician experienced in HIV care.
7. If the alleged assailant has been confirmed to be HIV-infected, take into consideration CD4 cell level, viral

load, history of using ART's and resistance testing in the past must be taken into consideration for choosing the correct regimen. Initiation PEP immediately.

When to Initiate Therapy:

Important factors to be discussed when you consider initiation of treatment in a sexual assault victim: these are

- Potential benefit, unproven efficacy, and potential toxicity of PEP
- Duration of PEP regimen
- Importance of adherence to the treatment regimen to prevent PEP failure or the development of drug resistance should infection occur
- Need to reduce risk and prevent exposure to others (use of condoms during a period of 6 months)
- Clinical and laboratory monitoring and follow-up schedule
- Signs and symptoms of acute HIV infection

HIV Testing o f the Victim:

Baseline HIV testing of the victim identifies individuals who were already infected with HIV at the time of presentation. This allows for a decision to be made for initiating ART and not PEP.

Follow up of the Patient:

HIV testing	Timeframe for PEP	Regimen	Other drugs therapy	Duration
baseline rapid HIV testing on contact follow up at 2 and 4 months VDRL at 1 month	Within the first 4 hours follow up at 24 hours (emotional and psychological support) PEP beyond 36 hours post exposure should be made on an individual case scenario as efficacy decreases with the delay in time. If the victim is not able to make a decision offer a starter pack and follow up in 24 hours. A written form for consent or refusal to start PEP must be signed.	**Tenofovir/emtricitabine (TDF/FTC 300 mgs/200 mgs qid) or as an alternative** **Zidovudine/lamivudine (ZDV/3TC 300 mgs/150 mgs bid)+EFV- 600 mgs qid))** **Zidovudine/lamivudine (ZDV/3TC 300 mgs/150 mgs bid)+ Lopinavir /ritonavir (LPV/r 200 mgs/100 mgs bid)**	Emergency contraception should be discussed and offered within 72 hours of the assault. Prophylaxis for gonococcal and chlamydial infections	PEP duration is 4 weeks.

Pediatric HIV Care

The implementation of the PMTCT programme has resulted in a reduction of pediatric HIV infection and quality HIV care continues to be provided to children who are infected with HIV.**NOTE : Please refer to PMTCT guidelines**

When to Start ART in Adolescents and Children?

(ART) must be given to all HIV-infected children, regardless of clinical symptoms, VL or CD4 count.

Table 16: Preferred and Alternative First Line ART Regimens

Situation	Preferred 1st line regimen	Suggested alternative first line	Preferred 2nd line regimen being indicated as 1st line
Children more than 3 years	**AZT + 3TC + NVP** **FTC + 3TC + EFV**	**AZT+3TC+ABC** **TDF+3TC+LVP/r** **TDF+FTC+EFV**	**TDF + FTC + LPV/r** **AZT + 3TC + LPV/r**
Children less than 3 years	**ABC+3TC+LPV/r** **AZT+3TC+LPV/r**		
Child or adolescent with TB	**AZT+3TC+EFV**		
Adolescent with hepatitis B	**TDF + 3TC + NRTI** **TDF +3TC + EFV**		

Source: Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection What's new? WHO. November 2015

Clinical and Laboratory Monitoring in Children: Table 20

As part of an adequate clinical monitoring in children, the following should be performed:

1. Growth, development and nutrition should be monitored monthly.
2. A baseline chest radiograph to allow assessment for respiratory complications, including lymphoid interstitial pneumonitis and TB.
3. Immunization should be administered as per PMTCT guidelines**. See Annex 9**

Table 17: Laboratory Tests for HIV-Infected Children(source)

Laboratory Test	Frequency
CD4 Count	❖ At the time of diagnosis of HIV infection ❖ Every 3 months ❖ If new clinical staging events develop or there is a failure to thrive clinically ❖ Every 12 months in children and adolescents who are adherent to therapy and have stable CD4 cell levels
Viral Loads	❖ As required or every six months ❖ should be performed to confirm clinical or immunological failure
FBC, Platelets & hemoglobin	❖ At the time of diagnosis and repeat in 2-4 weeks and then every 3 months for the first 2 years
Liver Function Tests	❖ At the time of diagnosis and repeat in 2-4 weeks and then every 3 months (for the first 2 years): SGOT, SGPT, Total Bilirubin, Direct Bilirubin, Total Protein ❖ Hepatitis B screening must be performed before start ART
Kidney Function Tests	❖ Every 3 months: BUN, Creatinine
Electrolytes	❖ Potassium, Sodium, Chloride every 3 months
NOTE: ****If child is on 2nd Line Regimen: also check cholesterol, triglyceride, uric acid, alkaline phosphate and amylase every 3 months.** ****Urinalysis every 12 months, Tuberculin skin test every 12 months, electrocardiogram/echocardiogram every 3 to 5 years.** ****If lipids have been abnormal in the past, more frequent monitoring might be needed.** ****Kidney function tests should be performed in Patients receiving TDF.**	

Adherence in Children

Regardless of their severity, adverse reactions may influence adherence to therapy. Parents, guardians and the patient must be informed of potential side-effects before starting ART. These drug toxicities maybe time-limited, resolving spontaneously without discontinuing the ART.

Support should be offered during these minor or moderate adverse reactions, to ensure adherence to therapy. Severe reactions are (e.g. NVP-associated Steven – Johnson syndrome, drug-induced hepatitis, lactic acidosis, pancreatitis, or ABC-associated hypersensitivity).

Recommendations:

- ❖ Strategies to improve and maintain adherence should be discussed before initiation of ARV and before changing regimens
- ❖ Assess and promote adherence to therapy on every visit (at least 1 method)
- ❖ adherence to antiretroviral can be measured by the monitoring of viral load levels
- ❖ If possible once-daily antiretroviral regimens should be prescribed (FDCs)

- Providers should have a nonjudgmental attitude to build and establish trust, with the patient
- If possible home visits can be programmed to assess adherence, family support, challenges etc.
- Choose the most palatable medicine possible
- Assess pill swallowing capacity and offer pill swallowing training aids (pill swallowing cup, pill glide)

HIV Drug Resistance in Children

Treatment failure can be classified as:

- Virologic failure: When there is an incomplete initial response to ART or when a viral rebound is seen after viral suppression had been achieved and can be described as a repeated viral load >200 copies/ml after 6 months of therapy (some infants with high viral load may take longer than 6 months to achieve viral supression).
- Immunonologic failure is defined as a suboptimal immunological response to ART during the course of treatment,
- Clinical failure: Clinical evidence of HIV disease progression during ART or the manifestation of a new opportunistic infection while on ART

Virologic suppression: is defined when a patient has a plasma viral load below the lower level of detection using highly sensitive assays with lower limits of quantitation of 20-75 copies/ml.

Virologic treatment failure is associated with: **poor adherence, drug resistance, poor absorption of medications, inadequate dosing, and drug-drug interactions therefore all of these factors must be strictly evaluated.**

Note : In children who complete 3 years of age and need to be switched to another regimen ensure that

1. the client has no adherence issues

2. That there is no evidence of clinical AEs within 2 weeks of starting new regimen

3. ensure that there is viral suppression and CD4 count consistently above >300

cells/mm

4. evaluate for evidence of viral load suppression at 4 weeks and CD4 at 2-8 weeks after new regimen is started

5. repeat liver function test and other routine test screening for toxicity

When to Switch to Second Line Regimen:

- ARV regimens should be chosen based on treatment history (drug-resistance testing,current and past resistance) test results
- New regimens should include at least two, but preferably three, antiretroviral medications with assessment of anticipated antiretroviral activity and past treatment history that includes resistance test results
- The goal of therapy following treatment failure is to achieve and maintain virologic suppression, being monitored via plasma viral load testing
- If virologic suppression cannot be achieved, the goals of therapy are to preserve or restore immunologic function (measured by CD4 cell levels), prevent clinical disease progression, and to avoid the development of additional drug resistance.

Considerations for Second and 3rd Line Regimens in Children see Table 19

NOTE: In the event of 2nd or 3rd line regimen failure, each case should be reviewed on an individual basis by a select team which will be providing recommendations for the best alternative regimen to be used.

Management of drug Toxicity or Intolerance:

- In the case of mild to moderate or transient side effects symptomatic treatment must be used
- Management of toxicity of alternative drugs must be individualized according to the severity of the reaction, the need for further viral suppression and the availability of drugs.
- In the presence of severe or life-threatening toxicity (e.g., a hypersensitivity reaction), all antiretroviral (ARV) drugs should be suspended immediately. Once symptoms of toxicity have resolved, resume antiretroviral therapy by substituting the offending drugs or agent.
- When modifying therapy because of toxicity or intolerance to a specific drug in children with virologic suppression, changing one drug in a multidrug regimen is permissible; if possible, an agent with a different toxicity and side-effect profile should be chosen
- The toxicity and the medication presumed responsible should be documented in the medical record and the caregiver and patient advised of the drug-related toxicity
- Dose reduction is not a recommended option for management of ARV toxicity, except for those few ARV drugs (e.g.,efavirenz) for which a therapeutic range of plasma concentrations detected by therapeutic drug monitoring correlates with toxicity

See WHO Clinical Staging for HIV Infection in Children (> 15 years) for other conditions and diseases.

Special Consideration for Opportunistic Infections in Children (Tuberculosis)

Isoniazid Preventive Therapy (IPT)

- All HIV-infected infants and children exposed to TB through household contact, but with no evidence of active disease, should begin isoniazid preventive therapy (IPT).
- Children with HIV (older than 12 months of age and including those previously treated for TB), who do not have active TB, and are not known to be exposed to TB, should receive 6 months of IPT.
- HIV positive infants, who **DO NOT** have active TB and are **NOT known** to have been exposed to TB, should **NOT receive IPT**.
- Isoniazid (INH) as IPT in HIV co-infection is 10 mg/kg/d for 6 months (max 300 mg/day).

Infants and Children Diagnosed with TB and HIV Co-Infection

Any child with active TB disease should begin TB treatment immediately, and should start ART as soon as tolerated and within the first 8 weeks of having started TB therapy, irrespective of their CD4 count and/or clinical stage.

- The preferred first-line ARV regimen for infants and children less than 3 years of age, who are taking a rifampicin-containing regimen for TB is ZDV + 3TC + NVP.
- The preferred first-line ARV regimen for children more than 3 years of age who are taking a rifampicin-containing regimen is ZDV + 3TC + EFV.

For all HIV-infected children, anti-TB therapy should be started immediately upon the diagnosis of TB; and ART should continue as per prescribed regimen. Make adjustments to ART regimens as needed to decrease the potential for toxicities and drug interactions:

- If on a regimen of 2 NRTIs + NVP, substitute EFV for NVP if child is 3 years of age.
- If on a regimen of 2 NRTIs + NVP and substitution with EFV is not possible, ensure NVP is dosed at the maximum dose of 200 mg/m^2 per dose twice daily.
- If on a regimen of LPV/r, consider adding RTV to a 1:1 ratio of LPV r to achieve the full therapeutic dose of LPV. Regimen for TB is 2 NRTIs + EFV.

Prophylaxis to Prevent Opportunistic Infection in Children

Pneumocystis Pneumonia (PCP)

NOTE: HIV infected infants 1 -12 months: prophylaxis is indicated for **all** regardless of CD4 count or clinical status.

1 -5 years with CD4 count <500
6 -12 years with CD4 count <200

Table 18: Co-trimoxazole** (Trimethoprim/sulfamethoxazole) prophylaxis **dosage for children

Co-Trimoxazole dosage—single dose per day				
Age	**Weight**	**Suspension:**(40mg TMP/200mg SMX per 5ml)	**Adult Tablet:** (80mg TMP/400mg SMX)	**Adult Tablet:** (80mg TMP/400mg SMX)
<6months	<5kg	2.5ml	-	-
6months – 5yrs	5-15kg	5ml	½ tablet	-
6 -14yrs	15-30kg	10ml	1 tablet	½ tablet
>15 yrs	>30kg	NIL	2 tablet	1 tablet

See WHO, UNIAIDS and UNICEF modify recommendations for cotrimoxazole prophylaxis in children

Mycobacterium Avium (Azithromycin is used)

Table 19: Azithromycin dosing in children

Age	**Weight**	**Dosage**
≥6 yrs with CD4 count <50	<5 kg	20 mg/kg
2 yrs to 5 yrs with CD4 count <75	5-15 kg	20 mg/kg
1 yr to 2 yrs with CD4 count <500	15-30 kg	20 mg/kg
<1 yr with CD4 count <750	>30 kg	20 mg/kg

Ectended release patients <34 kg: 60 mg/kg (max dose2g/dose) orally as a single dose
Patients>34 kg 2g orally as a single dose

NOTE: The Formula for figuring out Body Surface Area (BSA):
Ht (cm) Wt (kg) then take the square root (√) of this number to get the BSA. **If no Height is available another formula can be used that is usually quite close to the actual BSA is: Wt (kg) x 4 + 7;** Wt (kg) +9

Combination therapy with two drugs azithromycin or clarithromycin plus ethambutol, is recommended to prevent or delay the emergence of resistance

The use of rifabutin is controversial

Annex 1: Grief and Loss in the Context of HIV and mental disorders:

Grief is an expected multifaceted response to any type of loss including death, and may be influenced by individual, cultural, religious, familial, community and social factors that surrounds the affected person.

Complicated grief: is defined as a prolonged period of intensified sorrow and distress that disrupt daily functioning.

Clinicians may have trouble distinguishing grief and bereavement from depression. Therefore these patients must be referred to a psychiatric specialist or psychiatric nurse.

Common symptoms of grief include:

1. **Emotional:** enduring sadness, shock, anger, anxiety, loneliness, yearning, guilt, fear, withdrawal, feeling worthless, apathy, irritability, appetite disturbances
2. **Physical**: fatigue, tightness in the chest, shortness of breath, lack of energy, numbness, nausea, body aches, panic attacks, insomnia
3. **Psychological/cognitive**: disbelief, confusion, sense of presence, lack of concentration, auditory hallucinations (hearing the voice of the deceased), intrusive thoughts, anxiety about death, mental fatigue
4. **Spiritual distress**: questioning faith or the meaning of being a survivor
5. Explore the nature and relationship of the loss/death and its impact
6. Assess if the grief reaction is appropriate for the setting/cultural context

Therefore, a person with living with HIV must be properly and carefully evaluated for signs and symptoms of any mental health issues utilizing a diligent medical history and a detailed clinical evaluation. Care and support should be delivered by a multidisciplinary team with a tailored individualized plan for care according to the particular condition of each patient.

Screening: As patients may not talk about their mental status, clinicians must routinely screen by asking the following questions:

Depression screening questions:

- How have you been in the past month/since your last visit?
- Have you been feeling more stressed than usual?
- Have you been feeling down, or low, heart-sore or depressed?

Gender based violence:

- How are things going in your relationship with your partner?
- Have you ever been emotionally, verbally, sexually or physically victimized?

Some patients on ART will need additional scrutiny if:

- They are responding poorly to ART (detectable viral load (VL)/may have adherence issues)
- They are exhibiting worrisome behavior (looking anxious/depressed, expressing suicidal ideation or self-harm).

Risk Assessment:

Clinicians should always assess for suicidal risk and tendencies in patients with depressive symptoms. **A patient is classified as High risk if he/she has:**

- a clear plan for ending life
- identified a deadly method to end life
- a previous suicide attempt
- lack of social support
- severe (psychotic) depressive disorder.

Mental State Assessment: Clinicians must perform and document a "mental state examination: looking closely at the appearance and behavior of the individual for example grooming, eye contact, motor activity, etc.

- level of consciousness: orientation in time, place or person.
- cognitive function
- mood: objectively euthymic (non depressed, reasonably positive mood), depressed, —manic tendencie
- speech, form and content of thinking: flow of speech, coherence and content of thinking (delusions, pre-occupations, ruminations)
- perceptual abnormalities: evidence of hallucinations
- insight into his/her own condition

Depressive Disorders

Depression can be evident in persons with poor self-care, adherence issues, lack of willingness to carry out daily chores) as thesecontribute to poor health outcomes. Suspect major depression if five or more of the following symptoms exist for more than 2 weeks:

Depressed mood almost all day/ every day

- Or loss of interest or enjoyment of usually pleasurable activities for most of the day

- Significant weight loss when not dieting or due to medical illness, or weight gain (e.g. >5% body weight change in a month), or decreased/increased in appetite
- Insomnia or hypersomnia, psychomotor agitation or retardation (observable by others, not merely subjective feelings of restlessness or of being slowed down)
- Fatigue or loss of energy
- Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) – not merely self-reproach or guilt about being sick
- Diminished ability to think or concentrate, or indecisiveness (either by sub-jective account or as observed by others)
- recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

Severe depression may present with psychotic symptoms such as delusions with feelings of (guilt, negativity, death, paranoia) and transient occasional hallucinations.

Management includes: Supportive Counselling for mild Depression

1. Psycho-education with the following key messages:
A. Depression is common and can happen to anyone
B. Depressed people may have exaggerated negative opinions about themselves, their life and their future
C. Effective treatment if is possible

Self-management includes:

1. To continue ART as prescribed
2. To enroll and continue participating in activities that patients find interesting/pleasurable
3. Have a regular sleeping cycle
4. Keep physically active
5. Participate in community/social events
6. Return if any thoughts of self-harm are present

Severe Mental Disorders and HIV

HIV positive individuals worldwide and in Belize may present with the following mental disorders (Schizophrenia, Bipolar mood disorders and Major depression disorders). These conditions may increase a persons risk of acquiring and transmitting HIV, as well as abandoning psychiatric treatment and ART.

The management of severe mental disorders requires a multidisciplinary team approach,with the establishment and use of support groups who will be involved and implement outpatient counselling, monitoring, education and registration with follow up of drug side effects and drug interaction in patients using ARVs.

Addressing psychosocial stressors:

1. Explore potential stressors in the patient's life
2. Assist in problem-solving to reduce stressors
3. Assess for and manage gender-based violence
4. Reactivation of referral system and identifying support groups
5. Regular follow up until patient is stabilized
6. Follow up of these patients with supportive counseling plus regarding medications and evaluation by psychiatry

Hospitalization Criteria in Patients with Major Depression:

1. High suicide risk upon evaluation
2. In complex cases: the presence of psychosis and/or minimal social support and/or a poor response to out-patient treatment and/or a diagnostic dilemma
3. In complex medical comorbidity (to monitor antidepressant medication)
4. In the event of severe psychomotor retardation or not eating/drinking.

Alcohol and Drug Use/Addiction:

It is important to note that adults and adolescents should be screened for alcohol and drug use before initiating ART and every 1-2 years by asking the following three questions:

1. During the past 12 months, did you drink any alcohol (more than a few sips)?
2. During the past 12 months, did you smoke any marijuana?
3. During the past months, did you use anything else to get high?

Annex 2: Adverse effect in considering using NVP and EFV

Difference	Nevirapine	Efavirenz
Rash, Stevens Johnson, Hepatoxicity at CD4 < 350 cells	+++	+
Daily Dose	Twice	once
Teratogenicity	(-)	(+)
Exacerbation of Psychiatric condition (Depression)	(+)	(+++)
Interaction with Rifampicin	(++)	(-)
Dizziness - Hallucinations	(+)	(+++)

Annex 3: Dosages of Recommended Antiretrovirals

Generic name	Dose
Nucleoside reverse transcriptase inhibitors (NRTIs)	
Abacavir (ABC)	300 mg twice daily or 600 mg once daily
Emtricitabine (FTC)	200 mg once daily
Lamivudine (3TC)	150 mg twice daily or 300 mg once daily
Zidovudine (AZT)	250−300 mg twice daily
Nucleotide reverse transcriptase inhibitors (NtRTIs)	
Tenofovir	300 mg once daily[1]
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	
Efavirenz (EFV)	600 mg once daily/400 mgs daily (EFV_{400})
Etravirine (ETV)	200 mg twice daily
Nevirapine (NVP)	200 mg once daily for 14 days, followed by 200 mg twice daily[2]
Proteases inhibitors (PIs)	
Atazanavir + ritonavir (ATV/r)	300 mg + 100 mg once daily
Darunavir + ritonavir (DRV/r)	600 mg + 100 mg twice daily
Fos-amprenavir + ritonavir (FPV/r)	700 mg + 100 mg twice daily
Indinavir + ritonavir (IDV/r)	800 mg + 100 mg twice daily
Lopinavir/ritonavir (LPV/r)	400 mg + 100 mg twice daily[3]
	Considerations for individuals on TB therapy In the presence of rifabutin, no dose adjustment required In the presence of rifampicin; use ritonavir super boosting (LPV 400 mg + RTV 100 mg twice daily) or LPV 800 mg + RTV 200 mg twice daily, with close clinical and hepatic enzyme monitoring
Integrase strand transfer inhibitors (INSTIs)	
Raltegravir (RAL)	400 mg twice daily

Source: Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: Recommendations for a public health approach, 2nd edition, WHO 2016

[1]TDF dosage adjustment for individuals with altered creatinine clearance (using Cockcroft-Gault formula).
Creatinine clearance ≥50 ml/min, 300 mg once daily.
Creatinine clearance 30−49 ml/min, 300 mg every 48 hours.
Creatinine clearance ≥10−29ml/min (or dialysis), 300 mg once every 72−96 hours.
Cockcroft-Gault formula: *GFR = (140-age) * (Wt in kg) * (0.85 if female) / (72 * Cr)*
[2]In the presence of rifampicin, or when patients switch from EFV to NVP, no need for lead-in dose of NVP.
[3] LPV/r can be administered as 4 tablets once daily (i.e. LPV800 mg + RTV 200 mg once daily) in patients with less than three LPV resistance-associated mutations on genotypic testing. Once-daily dosing is not recommended in pregnant women or patients with more than three LPV resistance-associated mutations.

Annex 4: Toxicities and Recommended Drug Substitutions

ARV	Common associated toxicity	Suggested substitute

drug		
TDF	Asthenia, headache, diarrhoea, nausea, vomiting, flatulence Renal insufficiency, Fanconi syndrome Osteomalacia Decrease in bone mineral density Severe acute exacerbation of hepatitis may occur in HBV co-infected patients who discontinue TDF	**<u>If used in first-line therapy</u>** **AZT** **<u>If used in second-line therapy</u>** **Within a public health approach, there is no option If patient has failed AZT/d4T in first-line therapy. If feasible, consider referral to a higher level of care where individualized therapy may be available**
AZT	Bone marrow suppression: macrocytic anemia or neutropaenia Gastrointestinal intolerance, headache, insomnia, asthenia Skin and nail pigmentation Lactic acidosis with hepatic steatosis Lipodistrophy	**<u>If used in first-line therapy</u>** **TDF**
EFV	Hypersensitivity reaction Stevens-Johnson syndrome Rash Hepatic toxicity Persistent and severe CNS toxicity (depression, confusion) Hyperlipidaemia Male gynaecomastia Potential teratogenicity (first trimester of pregnancy or women not using adequate contraception)	**NVP** **bPI if intolerant to both NNRTIs** **Triple NRTI if no other choice**
NVP	Hypersensitivity reaction Stevens-Johnson syndrome Rash Hepatic toxicity Hyperlipidaemia	**EFV** **bPI if intolerant to both NNRTIs** **Triple NRTI if no other choice**
ATV/r	Indirect hyperbilirubinemia Clinical jaundice Prolonged PR interval — first degree symptomatic AV block in some patients Hyperglycaemia Fat maldistribution Possible increased bleeding episodes in individuals with haemophilia Nephrolithiasis	**LPV/r**
LPV/r	GI intolerance, nausea, vomiting, diarrhoea Asthenia Hyperlipidaemia(especially hypertriglyceridemia) Elevated serum transaminases Hyperglycaemia Fat maldistribution Possible increased bleeding episodes in patients with haemophilia PR interval prolongation QT interval prolongation and torsade de pointes Risk of Myocardial infarction	**ATV/r**

The more serious overdose outcomes have been reported in neonates who were inadvertently administered suprahepatic doses of HIV prophylaxis medications(refer to PMTCT guidelines.

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Annex 5: ARV related Adverse events and Recommendations Symptom-directed toxicity management table

Adverse events	Major first-line ARVs	Recommendations

Acute pancreatitis	d4T	Discontinue ART. Give supportive treatment with laboratory monitoring. Resume ART with an NRTI with low pancreatic toxicity risk, such as AZT or TDF.
Drug eruptions (mild to severe, including Stevens-Johnson syndrome or toxic epidermal necrolysis)	NVP, EFV (less commonly)	In mild cases, symptomatic care. EFV rash often stops spontaneously after 3−5 days without need to change ART. If moderate rash, non-progressing and without mucosal involvement or systemic signs, consider a single NNRTI substitution (i.e. from NVP to EFV). In moderate and severe cases, discontinue ART and give supportive treatment. After resolution, resume ART with a bPI-based regimen.
Dyslipidemia	All NRTIs (particularly d4T) EFV	Consider replacing the suspected ARV
Anemia and neutropenia	AZT	If severe (Hb <7.0 g/dl and/or ANC <750 cells/mm^3), replace with an ARV with minimal or no bone marrow toxicity (e.g. d4T or TDF) and consider blood transfusion
Hepatitis	All ARVs (particularly NVP)	If ALT is at more than five times the basal level, discontinue ART and monitor. After resolution, restart ART, replacing the causative drug (e.g. EFV replaces NVP).
Lactic acidosis	All NRTIs (particularly d4T)	Discontinue ART and give supportive treatment. After resolution, resume ART with TDF.
Lipoatrophy and lipodystrophy	All NRTIs (particularly d4T)	Early replacement of the suspected ARV drug (e.g. d4T for TDF or AZT)
Neuropsychiatric changes	EFV	Usually self-limited, without the need to discontinue ART. If intolerable to the patient, replace NVP with EFV or bPI. Single substitution recommended without cessation of ART.
Renal toxicity (renal tubular dysfunction)	TDF	Consider substitution with AZT
Peripheral neuropathy	d4T	Replacement of d4T with AZT, TDF. Symptomatic treatment (amitriptyline, vitamin B6).

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annex 6: CDC Immunization Recommendations

1. Vaccinate according to national guidelines for healthy population, preferably after having achieved suppressed viremia and immune reconstitution (CD4 count > 200 cells/μL) giving vaccinnations to people living with HIV does not accelerate the progression of the disease
2. Consider repeating vaccinations performed at CD4 count < 200 cells/μL (< 14%) following adequate immune reconstitution (HIV-VL undetectable and CD4 count > 200 cells/μL)
3. As vaccine responses may be significantly lower in HIV-positive individuals, consider antibody titers to assess their effectiveness
4. Avoid polysaccharide vaccination. Patients suffering from severe immunosuppression may have higher risk of complications from some live attenuated vaccines

Immunization Schedule for Human Immunodeficiency Virus (HIV) –Infected Adults

Vaccine ⬇ Indication ➡	HIV Infection CD4+lymphocyte count < 200 cells/pt	HIV Infection CD4+ T lymphocyte count ≥ 200 cells/pt
Influenza*	1 Dose IIV + Annually	
Tetanus, diphtheria, pertussis (Td/Tdap)*	Substitute 1-time dose of Td booster; then boost with Td every 10 yrs	
Varicella*	**Contraindicated**	2 doses
Human papilloma virus (HPV) Female*	3 doses through age 26 yrs	
Human papilloma virus (HPV) Male*	3 doses through age 26 yrs.	
Zoster	**Contraindicated**	
Measles, mumps, rubella (MMR)*	**Contraindicated**	1 or 2 doses
Pneumococcal polysaccharide (PPSV23)	1 dose followed by a booster at 5 years	
Pneumoccocal 13-valent m conjugate (PCV13)*	1 dose	
Meningiococcal*	1 or more doses	
Hepatitis A*	2 doses	
Hepatitis B *	3 doses	

*Covered by the Vaccine Injury Compensation Program

Gv-Inactivated Influenza Vaccine, LAIV (live attenuated influenza vaccine) is not recommended for HIV-infected persons.

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection;

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

No recommendation

Adopted from the Advisory Committee on Immunization Practices (ACIP) 2013 Adult Immunization Schedule A Summary of the adult immunization schedule vaccines and their primary indications, adverse events and contraindications can be found at: wwwcdc.gov/vaccines/schedules/download/adult/mmwr-adult-schedule.pdf. for more detailed information on immunization of persons with hIV infection against influenza, pneumococcal disease, hepatitis B, human papilloma virus, varicella and hepatitis A, see disease-specific sections in the text and in Table 1. For additional information on these and other vaccines (tetanus, diphtheria, pertussis, measles, mumps, rubella, and meningococcal disease), refer to recommendations of the ACP at www/cdc.gov/vaccines/pubs/acip-list.htm

Source: Centers for Disease Control and Prevention

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