HIV GUIDELINES 2018 SUMMARISED

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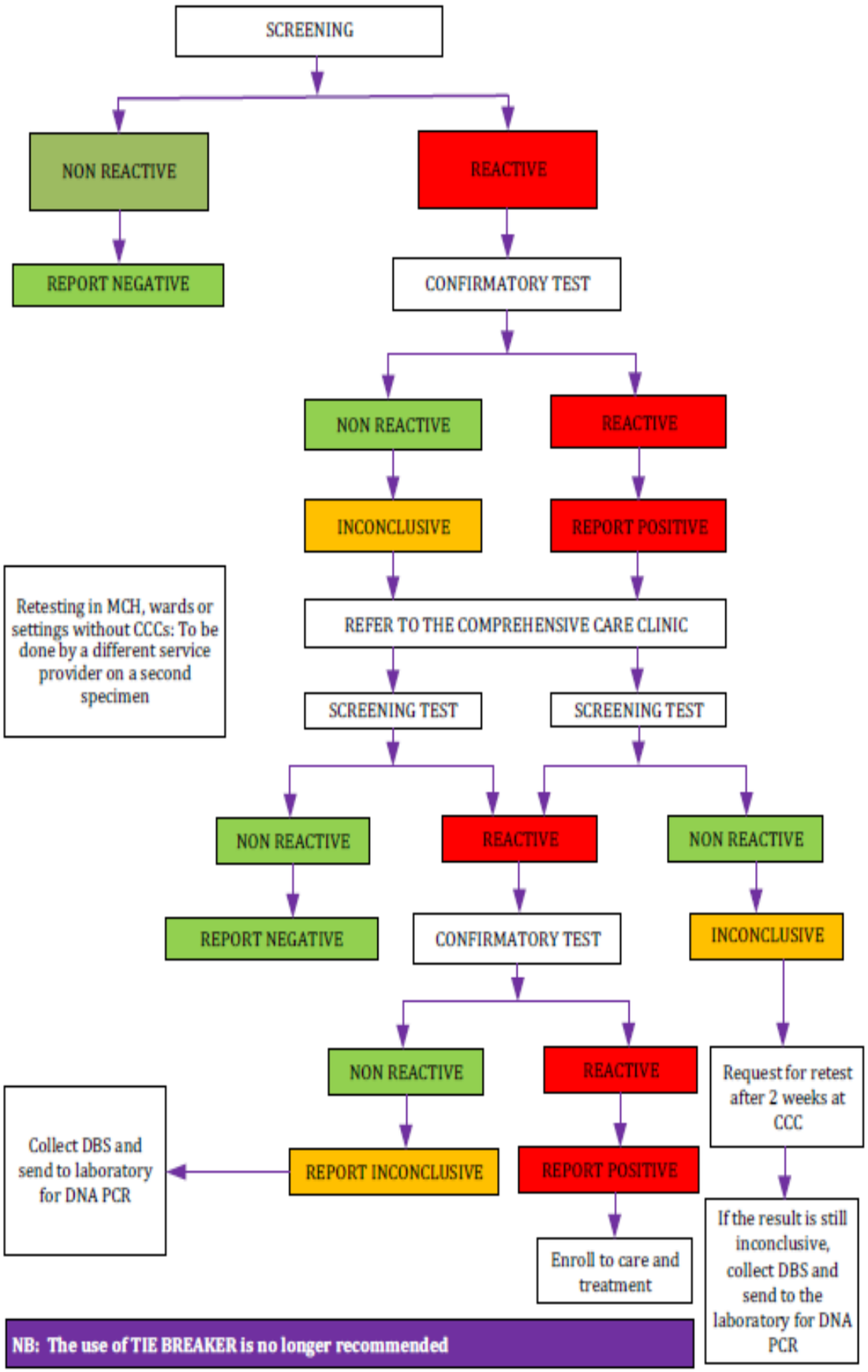

Figure 2.3: HIV Testing Services Algorithm

Stage 1 • Asymptomatic • Persistent Generalized Lymphadenopathy (PGL)	Stage 2 • Moderate unexplained weight loss (< 10% of presumed or measured body weight) • Minor mucocutaneous manifestations (seborrheic dermatitis, papular pruritic eruptions, fungal nail infections, recurrent oral ulcerations, angular cheilitis) • Herpes zoster • Recurrent upper respiratory tract infections (sinusitis, tonsillitis, bronchitis, otitis media, pharyngitis)
Stage 3 • Unexplained severe weight loss (over 10% of presumed or measured body weight) • Unexplained chronic diarrhoea for longer than one month • Unexplained persistent fever (intermittent or constant for longer than one month) • Persistent oral candidiasis • Oral hairy leukoplakia • Pulmonary tuberculosis • Severe bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia) • Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis • Unexplained anaemia (below 8 g/dl), neutropenia (below 0.5 x 109/l) and/or chronic thrombocytopenia (below 50 x 109 /l)	Stage 4 Conditions where a presumptive diagnosis can be made using clinical signs or simple investigations: • HIV wasting syndrome • Pneumocystis jirovecipneumonia (PCP) • Recurrent severe bacterial pneumonia (≥ 2 episodes within 1 year) • Cryptococcal meningitis • Toxoplasmosis of the brain • Chronic orolabial, genital or ano-rectal herpes simplex infection for > 1 month • Kaposi's sarcoma (KS) • HIV encephalopathy • Extra pulmonary tuberculosis (EPTB) Conditions where confirmatory diagnostic testing is necessary: • Cryptosporidiosis, with diarrhoea > 1 month • Isosporiasis • Cryptococcosis (extra pulmonary) • Disseminated non-tuberculous mycobacterial infection • Cytomegalovirus (CMV) retinitis or infection of the organs (other than liver, spleen, or lymph nodes) • Progressive multifocal leucoencephalopathy (PML) • Any disseminated mycosis (e.g. histoplasmosis, coccidiomycosis) • Candidiasis of the oesophagus or airways • Non-typhoid salmonella (NTS) septicaemia • Lymphoma cerebral or B cell Non-Hodgkin's Lymphoma • Invasive cervical cancer • Visceral leishmaniasis • Symptomatic HIV-associated nephropathy or HIV associated cardiomyopathy

Table 3.1: Initial Clinical Evaluation for PLHIV (History and Physical Examination)

History		Comments
Current and past medical history	The initial visit provides the opportunity to establish a meaningful patient-provider relationship; the clinician should elicit concerns and expectations with open, non-judgmental and clear communication	
	• Presenting complaints/current symptoms • Include symptoms of TB and TB contacts	• Inquire about symptoms due to co-existing HIV-related and non-HIV-related disease and co-morbidities that will require immediate intervention • Completion of the Intensified Case Finding (ICF) tool
	• Date of first positive HIV test • Past and current co-morbidities (e.g. TB, cryptococcal meningitis, hypertension, diabetes, kidney and liver disease) • Current medications, including herbs • Drug allergies, especially sulfa allergy • ARV exposure history • History of hospitalizations • Family history of chronic disease or cancer	• Document history of TB • Document previous or current ARV use (including for PMTCT, PEP, PrEP and ART) • Establish current medications (prescription, non-prescription, and herbal) likely to adversely interact with ARVs • Establish reasons for hospitalizations
Psychosocial history	• Education, employment, family, marital status • Past treatment for mental illnesses; current symptoms of depression • Disclosure and self-stigma • Substance use including alcohol, tobacco, miraa (khat), marijuana, narcotics, injection drug use • Nutritional history and adequacy of nutritional intake and household food security	• Establish and document social support structures • Establish possible presence of mental health concerns • Encourage disclosure to trusted close relations/friends and sexual partners • Elicit and begin to address possible barriers to adherence • Link to additional facility and community support resources, including psychosocial support groups, peer mentors, harm reduction services for PWIDs, etc
Sexual and reproductive history	• Past history of STIs • Current symptoms of STIs • Sexual practices • Partner HIV status and disclosure to sexual partner(s) • Pregnancy history and age of all living children • Menstrual history, family planning and plans for pregnancy • History of cervical cancer screening	• Discuss secondary prevention and avoidance of re-infection with STIs • HIV and ART status of sexual partner/s • Discuss pregnancy intention and contraception needs • Encourage contact tracing and HIV testing for sexual partners and all children of HIV-infected women and all children whose mothers' HIV status is unknown

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Table 3.1 (Continued): Initial Clinical Evaluation for PLHIV (History and Physical Examination)

Physical Examination		Comments
General impression, vital signs and anthropometric measurements	Assess general mood, measure and record weight, height, MUAC (in children and pregnant women), temperature, pulse rate, BP, respiratory rate, pulse oximetry (if patient has respiratory complaints or has difficulty in breathing)	• Calculate BMI as: Weight (kg)/ Height^2(m) • Use z-scores for children • Monitor growth trends for children
General examination	Conjunctiva and palms for pallor or jaundice; swollen lymph nodes (cervical, axillary, inguinal); mouth (for Kaposi's sarcoma (KS) lesions, oral hairy leucoplakia, candidiasis, tooth decay); skin (for drug eruptions, herpes zoster, dermatitis, pruritic papular eruptions (PPE), folliculitis, fungal infections, molluscum, and KS)	• Prompt treatment of inter-current illness contributes towards success of ART and reduction in early morbidity and mortality • Asymmetric or rapidly enlarging lymph nodes will require fine needle aspiration cytology or biopsy • Cervical cancer screening (if not done in the past year), and appropriate management • Monitoring developmental milestones for children
Systemic examination	Central Nervous System (focal defects, retina); Mental State Examination (for mental status); abdomen (for liver or splenic enlargement); respiratory (for dullness to percussion; crackles or wheezes); cardiovascular (for peripheral pulses, oedema, heart sounds); if specific symptoms: genitourinary/ anorectal system (for ulcers, discharge, condylomata/warts, prostate examination for men ≥ 45 years of age). Speculum examination with cervical cancer screening for females	
Summary	Problem list with differential diagnosis and management plan for each problem (including investigations, treatment, referrals, and follow-up)	• Assign and document the initial WHO Clinical Stage and manage presenting illnesses • Growth and developmental milestone must be assessed and used for WHO staging in children • Differentiate between patients with advanced disease versus those who are clinically well, to guide acuity of follow-up

NOTE: Laboratory assessment is not a prerequisite to ART initiation. It should not cause a delay in starting ART

Table 3.2: Baseline Laboratory Investigations for PLHIV

	Test	Comments
HIV specific	Confirm and document positive HIV test result	• Refer to Figure 2.3
	CD4 cell count	• **Recommended at baseline for all patients** (CD4% for children ≤ 5 years old) • If CD4 ≤ 200 cells/mm^3 (for adults and adolescents) then laboratory should automatically perform a serum cryptococcal antigen (sCrAg) on the same sample to screen for cryptococcal infection
	Viral load (HIV-1 RNA)	• Baseline viral load (VL) is only recommended for HEIs after 1st PCR test is positive. Specimen for baseline VL can be drawn at the time of initiating ART; obtaining a VL should not delay ART initiation
	Serum Cryptococcal Antigen (sCrAg)	• Obtain serum CrAg in all adults and adolescents with a CD4 count ≤ 200 cells/mm^3. This should be done as reflex testing by the laboratory • If positive, manage as per the cryptococcal meningitis screening algorithm (Figure 4.1)
	HIV Drug Resistance Testing (DRT)	• Not currently recommended as a baseline investigation
Others	Hb (preferably full blood count if available)	• Recommended for all patients • If baseline Hb < 9.5 g/dL then AZT should be avoided
	Pregnancy status	• Pregnancy status should be determined for all women of reproductive age (based on history of last menstrual period, and if uncertain, irregular, or delayed then a urine pregnancy test should be performed)
	Urinalysis (for protein & glucose)	• Recommended for all patients

	Creatinine	• Recommended for all patients
		• Calculate Creatinine Clearance (CrCl), Annex 15
		  ○ If HBV negative and CrCL ≤ 50 ml/min then TDF should be avoided (Table 6.7)
		  ○ If HBV positive and CrCl ≤ 50 ml/min then TDF should still be used (Table 9.3)
		  ○ CrCl is also used for dose adjustment of NRTIs, CTX and fluconazole (Table 6.7)

	Syphilis serology (VDRL, TPHA, or RPR)	• Recommended for all PLHIV with a history of being sexually active

Table 3.2: (continued): Baseline Laboratory Investigations for PLHIV

	Glucose	• Recommended for all patients
	Plasma lipid profile	• Recommended for all patients
	HBsAg	• Recommended for all adolescent and adult PLHIV (plus children who did not complete routine childhood immunizations) • If negative, patients should be immunized for HBV as soon as they achieve confirmed viral suppression (see Section 4.8.1 and Section 9) • If positive refer to Section 9 for management of HIV/HBV co-infection
	HCV antibody	• Recommended for PWID or for patients with history of injection drug use
	ALT	• Not a recommended as baseline investigation unless there is a specific clinical reason (e.g. patient with history of hepatitis, signs or symptoms of liver disease, or risk of liver disease - alcoholics, HBV or HCV infection, hepatotoxic drugs such as fluconazole, etc)

6.1. Eligibility for ART

All individuals with confirmed HIV infection are eligible for ART irrespective of CD4 cell levels, WHO clinical stage, age, pregnancy or breastfeeding status, co-infection status, risk group, or any other criteria.

Population	Timing of ART Initiation	Comments
Pregnant and breastfeeding women	Support ART initiation on the same day as testing positive for HIV	Intensive adherence counselling and close follow-up required because of limited time for patient preparation
Infants (< 12 months old)	Support ART initiation on the same day as testing positive for HIV	Intensive adherence counselling and close follow-up required because of limited time for caregiver preparation
Patients with strong motivation to start ART immediately	Support ART initiation as soon as they meet ART Readiness Assessment criteria, even if on the same day as testing positive for HIV	Intensive adherence counselling and close follow-up required because of limited time for patient preparation
Patients with newly diagnosed TB	Start anti-TB treatment immediately and initiate ART as soon as anti-TB medications are tolerated, preferably within 2 weeks. For TB meningitis consider delaying ART for up to 8 weeks	Monitor closely for IRIS (Annex 16)
Patients with cryptococcal meningitis	Defer ART until after completing 5 weeks of CM treatment and symptoms have resolved	Monitor closely for IRIS (Annex 16)

≥ 15 years (**or** ≥ 35 kg body weight)	TDF + 3TC + DTG[8] **or** TDF + 3TC + EFV[9]	TDF/3TC/DTG (300/300/50mg): 1 tab once daily **or** TDF/3TC/EFV (300/300/400mg): 1 tab once daily

Age	Scenario and ARV Affected	Alternative ARV to Use
≥ 15 years (**or** ≥ 35 kg body weight)	TDF: Impaired renal function (CrCl ≤ 50 ml/min)	Use ABC
	DTG: Unable to tolerate DTG	Use EFV (for PWID who cannot tolerate DTG use ATV/r)
	DTG: Currently on anti-TB medications	Give TDF/3TC/DTG FDC am + DTG 50 mg pm for duration of rifampicin-containing TB treatment and for an additional 2weeks after TB treatment is completed then revert to TDF/3TC/DTG FDC OD [4]
	EFV 400 mg: Currently on anti-TB medications	Give TDF/3TC/EFV 400 mg FDC + EFV 200 mg for duration of rifampicin-containing TB treatment and for an additional 2weeks after TB treatment is completed then revert to TDF/3TC/EFV 400 mg FDC OD [4]
	EFV (for women and adolescent girls of childbearing potential) Unable to tolerate EFV (severe CNS side effects or moderate-severe rash); psychiatric history	Use ATV/r

6.4. Dosing and Administration of Dolutegravir (DTG)

DTG is preferred in first line ART in combination with two other ARVs for adolescents and adults. DTG is not recommended for women and adolescent girls of childbearing potential. Women and adolescent girls who are on effective contraception may opt to use DTG and should be support in their decision. DTG is well tolerated, has a high genetic barrier to resistance and fewer drug-drug interactions.

Table 6.4: Dosing and Administration of Dolutegravir

Recommended Dosing of DTG

- ≥ 15 years (**or** ≥ 35 kg body weight): DTG 50 mg once daily, preferably as a morning dose
- For patients taking rifampicin: increase dose to DTG 50 mg twice daily until 2 weeks after completion of TB treatment, then reduce to DTG 50 mg once daily again (the additional 2 weeks of higher-dose DTG is to counter the ongoing liver enzyme induction effect of rifampicin, which continues for a short period after TB treatment is completed)
- For patients with suspected or confirmed INSTI resistance (e.g. patients with prior history of failing a RAL-based regimen): use DTG 50 mg twice daily
- DTG can be taken with or without food
- Dosing guidance for children and adolescents < 35 kg will be provided once appropriate formulations are available

Common Side Effects of DTG

- The most common side effects of DTG are headache, nausea and diarrhea. These side effects usually resolve after continued use for 1-2 weeks. It is critical to inform patients about these potential side effects and their temporary nature, and encourage them to continue their ART and consult a HCW if concerned
- Some patients on DTG are more likely to develop insomnia. This may be reduced by taking DTG as a morning dose, or by taking DTG with a low-fat meal or on an empty stomach
- DTG may cause a small rise in serum creatinine levels but this does NOT represent a true decline in renal function
- All adverse events should be reported through the national pharmacovigilance mechanism (http://www.pv.pharmacyboardkenya.org/)

Pregnancy Safety of DTG

- DTG may be associated with increased risk of neural tube defects if taken around the time of conception. This potential risk is still under evaluation, but to be cautious DTG is not currently recommended for women with any childbearing potential
- DTG is safe during pregnancy and breastfeeding if initiated 8 weeks after conception (although women need to be counseled on the risk of becoming pregnant while breastfeeding and provided with effective contraception)

Important Drug Interactions with DTG

- Rifampicin
  - Rifampicin lowers DTG levels: increase DTG to 50 mg twice daily for patients on rifampicin
  - There are no significant drug interactions between DTG and other currently used anti-TB medications (including for MDR-TB)
- Mineral supplements, including: antacids containing calcium, zinc, magnesium or aluminum; iron supplements; prenatal vitamins (which contain iron and calcium)
  - These supplements decrease the absorption of DTG: administer DTG at least 2 hours before or 6 hours after taking any of these supplements
  - Dose separation is not required for calcium and iron supplements (including prenatal vitamins) if DTG is taken with a meal
  - **It is critical to educate patients about this important drug interaction because many patients get these supplements and antacids over-the-counter without informing their healthcare provider**
- Carbamazepine, phenobarbital, phenytoin
  - These anticonvulsants decrease DTG levels: use a different anticonvulsant if available
  - If DTG must be co-administered with these drugs then increase to DTG 50 mg twice daily, although there is little data to guide this
- Metformin
  - DTG increases levels of metformin; the levels of DTG are not affected: use a lower dose of metformin (often 50% of usual dose) and monitor glycemic control. Use a maximum daily dose of metformin 1 g
- Other drug-drug interactions with DTG
  - See Annex 13C

Contraindications for use of DTG

- DTG is not currently recommended for women and adolescent girls of childbearing potential
- DTG is contraindicated for any patient with a history of hypersensitivity reaction to DTG
- DTG is not currently recommended for patients with end-stage renal disease or end-stage liver disease because it has not been evaluated in these populations

Table 6.8: Common Significant Adverse Drug Reactions

ARV Agent	Adverse Drug Reaction	High Risk Situations/Comments
NRTIs		
ABC	ABC hypersensitivity reaction (see Table 6.10)	Do not re-challenge
AZT	Anaemia, neutropenia (see Table 6.8)	Risk factors: CD4 count < 200 cells/mm^3; BMI < 18.5 (or body weight < 50 kg); anaemia at baseline; concurrent use of other drugs with similar ADR (cotrimoxazole, gancyclovir, ribavirin)
	Lactic acidosis	Risk factors: Pregnancy; obesity
	Lipoatrophy	Risk factors: Low CD4 count
TDF	Renal dysfunction (see Figure 6.4)	Risk factors: Underlying renal disease; age > 40 years; BMI < 18.5 (or body weight < 50 kg); diabetes; hypertension; concomitant PI use or nephrotoxic drug
NNRTIs		
All NNRTIs	Rash/hypersensitivity (NVP>>EFV>ETR)	Risk factors: for NVP hypersensitivity, women with CD4 count > 250 cells/mm^3, men with CD4 count > 400 cells/mm^3 Manage rash as per Table 4.4
EFV	CNS side-effects	Risk factors: Pre-existing psychiatric disorder
	Gynaecomastia	Switch from EFV to an alternative, and consult if gynecomastia does not improve
NVP	Hepatotoxicity (see Table 6.9)	Risk factors: HBV or HCV co-infection; concomitant use of hepatotoxic drugs; women with CD4 count > 250 cells/ mm^3; men with CD4 count > 400 cells/mm^3
PIs		
All PIs boosted with RTV	GI intolerance (LPV/r>DRV/r>ATV/r)	Consult
	Dyslipidaemia (LPV/r>DRV/r>ATV/r)	Risk factors: Obesity; sedentary lifestyle; diet high in saturated fats and cholesterol
ATV/r	Hyperbilirubinemia	This only requires drug substitution if cosmetic effect of jaundice is likely to interfere with patient adherence
DRV/r	Rash/hypersensitivity	Risk factors: sulfa allergy
INSTIs		
DTG	Insomnia	Give in the morning; if no improvement then try giving with low fat meal or on empty stomach
All INSTIs	Rash/hypersensitivity	Consult

6.5.4. Changing ARVs Due to Treatment Failure

Viral load is the test of choice for monitoring response to ART and identifying treatment failure. Frequency of routine VL monitoring for specific populations is:

- Age 0-24 years old: every 6 months
- Age ≥ 25 years old: at 6 months after ART initiation, then at 12 months and then annually
- Pregnant or breastfeeding: at confirmation of pregnancy (if already on ART) or 3 months after ART initiation (if ART initiated during pregnancy/ breastfeeding), and then every 6 months until cessation of breastfeeding
- Before making any drug substitution (if no VL results from the prior 6 months)
- 3 months after any regimen modification (including single-drug substitutions), and then as per population group
- For any patient with a detectable VL follow the viral load monitoring algorithm (Figure 6.5)

Interpreting Viral Load Results and Defining Treatment Failure

The goal for ART is to achieve sustained viral suppression defined as below the Lower Detection Limit (LDL). The specific LDL value depends on the specimen type and assay used to measure VL.

Persistent low-level viremia (PLLV) is defined as having a detectable VL (above the LDL value but < 1,000 copies/ml) on two consecutive measures. These patients are at increased risk of progression to treatment failure, development of resistance and death and therefore require a similar case management approach as patients with VL ≥ 1,000 copies/ml (Figure 6.5)

Treatment failure is suspected when a patient has a high VL ≥ 1,000 copies/ml after at least 6 months of using ART. Treatment failure is only confirmed when VL is ≥ 1,000 copies/ml after assessing for and addressing poor adherence or other reasons for high VL, and then repeating VL after at least 3 months of excellent adherence to allow for viral re-suppression (Figure 6.5).

Note: Treatment failure should be suspected when a new or recurrent HIV associated condition indicating severe immunodeficiency (WHO stage III or IV condition) develops after at least 6 months on ART (excluding IRIS occurring after initiation of ART), or when CD4 count fails to rise as expected or when CD4 count drops while on ART. Treatment failure should always be confirmed with VL testing.

Clinical and immunological criteria for identifying treatment failure have low sensitivity and specificity for diagnosing treatment failure. Every effort should be made to obtain a viral load test.

Table 6.11: Recommended Second-line ART Regimens in Infants, Children, Adolescents and Adults, excluding TB/HIV co-infection [1]

Age/Scenario	First-line ART	Second-line ART
< 3 years	ABC (or AZT) + 3TC + LPV/r	DRT-based 2nd line[2]
	ABC + 3TC + NVP (or RAL)	AZT + 3TC + LPV/r
	AZT + 3TC + NVP (or RAL)	ABC + 3TC + LPV/r
3 - 14 years (and < 35 kg body weight)	ABC + 3TC + EFV (or RAL)	AZT + 3TC + LPV/r
	AZT + 3TC + EFV (or RAL)	ABC + 3TC + LPV/r
	ABC (or AZT) + 3TC + LPV/r	DRT-based 2nd line[2]
≥ 15 years (**or** ≥ 35 kg)	TDF (or ABC) + 3TC + DTG (or EFV)	AZT + 3TC + ATV/r[3]
	AZT + 3TC + DTG (or EFV)	TDF + 3TC + ATV/r[3]
	TDF (or ABC or AZT) + 3TC + ATV/r (or LPV/r)	DRT-based 2nd line[2]
Pregnant or Breastfeeding	TDF (or ABC) + 3TC + DTG (or EFV)	AZT + 3TC + ATV/r[3]
	AZT + 3TC + DTG (or EFV)	TDF + 3TC + ATV/r[3]
	TDF (or ABC) + 3TC + ATV/r (or LPV/r)	Take sample for DRT and change to AZT + 3TC + DRV/r + RAL; modify based on DRT results
	AZT + 3TC + ATV/r (or LPV/r)	Take sample for DRT and change to TDF + 3TC + DRV/r + RAL; modify based on DRT results
HIV/HBV Co-infection	Always maintain TDF in second-line instead of switching to a different NRTI and instead of adding an additional NRTI (e.g. if patient with HBV/HIV is failing TDF/3TC/DTG then switch to TDF/3TC+ATV/r)	
Contraindication to Recommended Second-line NRTI	Continue the first-line NRTIs while changing the other component to the recommended second-line ARV (e.g. if patient with anemia is failing TDF/3TC/DTG then switch to TDF/3TC+ATV/r)	
TB/HIV Co-infection	Refer to Table 8.7: Recommended ART Regimens for Patients who Develop TB while **Failing** 1st Line ART	

Table 6.12: Possible Third-line ART in Children, Adolescents and Adults

	Possible 3rd Line Regimen	Comment
Children	RAL (or DTG) + 3TC + DRV/r	DTG can be substituted for RAL in children once pediatric formulations of DTG are available and weight-based dosing bands are defined Regional or National HIV Clinical TWG may recommend reusing some of the ARVs the patient has already failed, even when resistance is present
	AZT + RAL (or DTG) + 3TC + DRV/r	
	ABC (or TDF) + RAL (or DTG) + 3TC + DRV/r	
	ETV + 3TC + DRV/r	
Adults	DTG + 3TC + DRV/r	
	DTG + AZT + 3TC + DRV/r	
	DTG + TDF + 3TC + DRV/r	
	DTG + TDF (or AZT) + 3TC	
	ETV + 3TC + DRV/r	

4.3.1. Cotrimoxazole Preventive Therapy (CPT)

All PLHIV should receive lifelong CPT (Table 4.3) unless they have an allergy to sulfa drugs or develop toxicity from CPT. For HIV exposed and infected infants, CPT should start at 6 weeks of age. CPT is effective in preventing specific OIs for patients with low CD4 counts (PCP and toxoplasmosis), as well as reducing the risk of common bacterial infections, sepsis, diarrhoeal illness and malaria.

Table 4.3: Daily Dose of Cotrimoxazole Preventive Therapy

Weight (kg)	If using oral suspension (240mg per 5ml)	If using single strength tablet 480	If using double strength tablet 960 mg
1 – 4	2.5 ml	¼ SS tab	--
5 – 8	5 ml	½ SS tab	¼ DS tab
9 – 16	10 ml	1 SS tab	½ DS tab
17 – 30	15 ml	2 SS tabs	1 DS tab
> 30	20 ml	2 SS tabs	1 DS tab
Adult (any weight)		2 SS tabs	1 DS tab

Note: If CrCl 15-30 ml/min then use 50% of normal recommended dose; if CrCl < 15 ml/min then CTX should be avoided

During pregnancy, CPT should be initiated irrespective of the gestational age and should continue throughout pregnancy, breastfeeding, and thereafter for life. Additional intermittent preventive therapy (sulfadoxine-pyrimethamine (SP)) for malaria is not required in women already on CPT.

Cotrimoxazole can cause anaemia and neutropenia in some patients, as well as a skin rash.

Dapsone as a Substitute for CPT

In situations of severe allergy to cotrimoxazole or when desensitization is not successful, dapsone can be used instead of CTX. It is primarily effective as prophylaxis against PCP but does not have the other prophylactic benefits of cotrimoxazole.

Dapsone will contribute to anaemia in most patients, and causes haemolytic anaemia in some patients, so patients should have a baseline Hb before starting dapsone and Hb monitored every 1-2 weeks for the first couple of months. Dapsone is not recommended during breastfeeding.

When dapsone (as a substitute for CPT) is being used as PCP prophylaxis, it is only recommended for patients in WHO Stage 4 and/or with absolute CD4 count ≤ 200 cells/mm^3 (or CD4 % ≤ 25% for children ≤ 5 years old), and should be discontinued once a patient achieves a sustained CD4 count of > 200 cells/mm^3 (or > 25% for children ≤ 5 years old) for at least 6 months.

Opportunistic Diseases

BACTERIAL	VIRAL	FUNGAL	PARASITIC	OTHER ILLNESSES
Tuberculosis	Varicella zoster	Candidiasis	Isosporiasis	AIDS -dementia
Bacterial respiratory infections	Oral leukoplakia	Cryptococcosis	Microsporidi-osis	Invasive cervical cancer
Bacterial enteric infections	HSV CMV	Penicilliosis	Cryptosporid-iosis	Non-Hodgkin's lymphoma
Pneumocystis jiroveci pneumonia	Human herpes virus type 8		Giardiasis Toxoplasmosis	Kaposi's sarcoma
Atypical mycobacteriosis	Human papilloma virus		Strongyloidiasis	

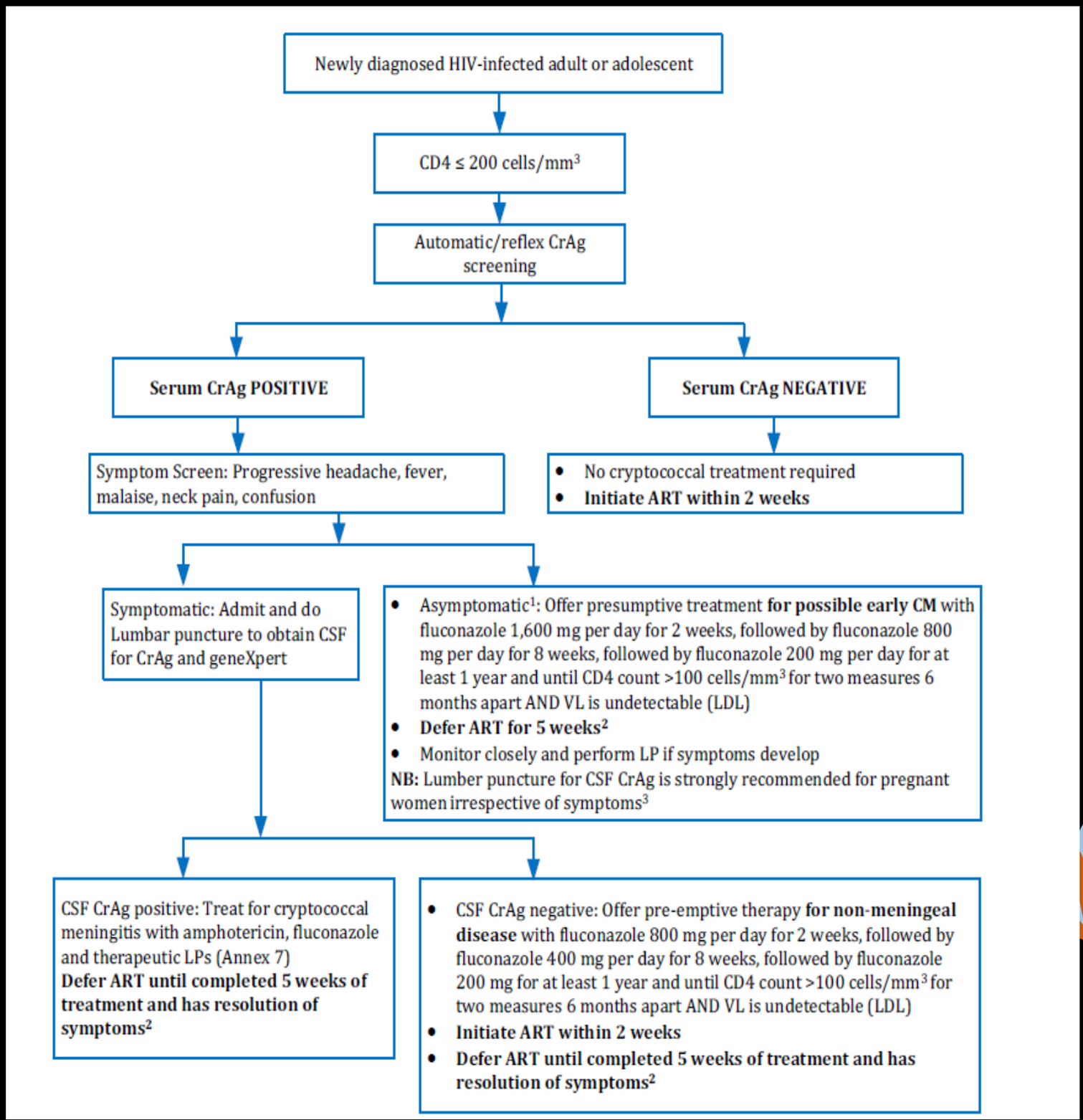
Table 1.1: CD4 and Risk of Opportunistic Infections and Conditions

CD4 Count (cells/mm³)	Likely Opportunistic Infections and Conditions
Any CD4	HIVAN, KS, TB
> 200	Bacterial pneumonia, TB, sensory polyneuropathy, HAD, PPE, thrush, EPTB
100- 200	Above plus PCP, EPTB
< 100	Above plus Toxoplasmosis, PML, NHL. Cryptococcal meningitis
< 50	Above plus MAC, CMV retinitis, , primary CNS lymphoma

HIVAN = HIV associated nephropathy; KS = Kaposi's Sarcoma; PPE = Papular Pruritic Eruptions; HAD = HIV associated dementia; EPTB = Extrapulmonary TB; PML = Progressive multifocal encephalopathy; NHL = Non-Hodgkin's Lymphoma;

MAC = Mycobacterium Avium Complex; CMV = Cytomegalovirus

CRYPTOMENINGITIS



[1]LP is recommended for all sCrAg positive patients irrespective of symptoms with management based on LP results. If LP is not available to rule out meningeal disease then patients should be treated for possible CM, even if asymptomatic

[2]Patients with cryptococcal meningitis are at high risk of developing life-threatening IRIS; deferring ART has been shown to improve survival for these specific patients

[3]Fluconazole use during pregnancy increases the risk of birth defects. All pregnant women who screen positive with serum CrAg should be offered a lumbar puncture (irrespective of symptoms) to determine if they have cryptococcal meningitis

Note:

- Fluconazole requires a dose adjustment for impaired renal function; when CrCl ≤ 50 ml/min then use 50% of the standard recommended dose
- Fluconazole should not be used with rifabutin-based TB treatment
- When using high-dose fluconazole check ALT after one week of treatment and based on symptoms thereafter

Annex 7: Treatment of Cryptococcal Meningitis

Target population	Regimen	Induction (2 weeks)	Consolidation (8 weeks)	Maintenance	When to start ART
Adults	Preferred	Ampho B 1.0 mg/kg/day + Fluconazole 1,200 mg/day	Fluconazole 800 mg/day	Fluconazole 200 mg/day for at least 1 year and until CD4 count > 100 cells/mm^3 for two measures 6 months apart AND VL is undetectable	Defer ART until after completing 5 weeks of CM treatment and symptoms have resolved
	Alternative	Fluconazole[1,2,3] 1,600 mg daily	Fluconazole 800 mg daily		
Children and adolescents	Preferred	Ampho B 1.0 mg/kg/day + Fluconazole 12 mg/kg/day (up to max 800 mg/day)	Fluconazole 6-12 mg/kg/day up to 800 mg/day	Fluconazole 6mg/kg/day up to 200 mg/day	
	Alternative	Fluconazole[1,2,3] 12 mg/kg/day (up to max 1,600 mg/ day)	Fluconazole 12 mg/kg/day up to 800 mg/day	Fluconazole 6mg/kg/day up to 200 mg/day	

[1]Fluconazole requires a dose adjustment for impaired renal function when CrCl ≤ 50 ml/min then use 50% of the standard recommended dose

[2]Flucozole should not be used with rifabutin-based TB treatment

[3]When using high-dose fluconazole check ALT after one week of treatment and based on symptoms thereafter

Managing and Monitoring for Amphotericin B Therapy

Adults

- Give 1 L of normal saline with 20 mmol of KCl over 2-4 hours before each controlled infusion of Ampho B given with 1 litre of 5% dextrose. Add one to two tablets of 8 mEq KCl orally twice daily. An additional one 8 mEq KCl tablets twice daily may be added in the second week. Include magnesium supplementation at 250 mg tablets of magnesium trisilicate twice daily (or 4 mEq tablets of magnesium chloride twice daily)

Adolescents and Children

- Give 1 L of normal saline with 20 mmol of KCl over 2-4 hours before each controlled infusion of Ampho B. Darrows or Ringer's solutions can also be used
- Avoid KCl replacement in patients with pre-existing renal impairment or hyperkalaemia

Managing hypokalaemia and raised creatinine levels

- Obtain a routine baseline and twice weekly potassium and creatinine:
  - If K < 3.3 mmol/L, administer 1 L of normal saline with KCl 40 mmol in normal saline or 1-2 tablets of 8mEq KCl every 8 hours. Add magnesium. Monitor potassium daily
  - If creatinine level increases > 2-fold from baseline, omit dose of Ampho B, increase hydration to 1 L every 8 hours. If there's improvement, re-start Ampho B at 0.7 mg/kg/day on alternate days. If no improvement, discontinue Ampho B, give fluconazole 1,600 mg/day to complete induction. Monitor creatinine daily

Pneumocystis Jerivocii pneumonia

Table 3.5: Summary of PCP Treatment

	Drugs	Dose
1st Line	Cotrimoxazole (Single strength, SS 400/80; double strength, DS 800/160) given for 21 days	20mg/kg of the trimethoprim component. (Alternatively, weight divided by 4 gives the number of SS tablets per 24 hr period)
2nd Line	Clindamycin *plus* Primaquine Pentamidine Given for 21 days	Clindamycin 600-900mg 8 hourly *plus* Primaquine 15-30mg/day Pentamidine 4mg/kg/day IV/IM
For the severely ill (O_2 saturation on air < 90%)	Add prednisolone from first day of treatment	40mg BD for 5 days, then 40mg daily for 5 days, then 20mg daily for the remaining 11 days

Table 4.1. Summary: HIV Associated Oral Lesions

Clinical condition	Presentation	Management
Candidiasis	White curd like patches on the tongue and inner surface of cheeks; can be easily scraped off revealing redness underneath. May also present as shiny erythematous patches or angular cheilitis	Nyastatin mouth drops 500000 units (5 ml) 4x per day for 7-14 days Miconazole gum patch **Systemic therapy if above fails:** Fluconazole 100 mg/day for 7 days Itraconazole 200mg/ day for 7 days (swished in mouth and swallowed on an empty stomach)
Apthous Ulcers	Ulcers in the mouth that are painful, are well defined with elevated margin and whitish floor	Antiseptic mouth washes (e.g. difflam) Local anaesthetic preparation prior to meals Corticosteroid preparations in oral gel 2° infection of ulcers is common requiring metronidazole + penicillin OR co-amoxiclav **For refractory cases:** Oral prednisolone (40mg per day for1-2 weeks before tapering) Dapsone 100mg /day **Resolves with ART.**

Table 4.1. Summary: HIV Associated Oral Lesions cont.

Clinical condition	Presentation	Management
Kaposi's Sarcoma	Lesions usually found on the roof of mouth or gums and do not hurt or itch; vary in colour from dark red, purple to brown. They start as patches then progress to thick bumps, to may become large tumours.	ART together with specific treatment of KS. Should be managed by an experienced clinician.
Oral Hairy Leukoplakia	Oral mucosal disease, associated with EBV, non-painful white plaque along the lateral tongue borders. Diagnosis is clinical.	Treatment not required.
HSV - 1	Painful, progressive anogenital or orolabial ulceration; More likely to recur or persist in PLHA	Aciclovir 400mg 8 hourly for 7-10 days

Table 4.2: Summary: Treatment of Oesophagitis in PLHA

Cause	Treatment
Oesophageal Candidiasis	**Preferred**: Fluconazole 200mg stat then 100mg OD PO x 14-21 days. IV if patient cannot swallow **Failure to improve on Fluconazole**: Increase dose to 400-800mg/day OR Itraconazole *solution* 200mg PO x 14-21 days OR Amphotericin B IV 0.3-0.7 mg/kg/day x 14-21 days If no response consider anti-HSV treatment
Herpes Simplex Virus (HSV) Oesophagitis	Aciclovir 800mg 6 hourly x 14-21 days Or Valaciclovir 1g PO TDS x 14-21 days
CMV Oesophagitis	Valganciclovir 900mg BD x 3 weeks
Aphthous Ulcers	Prednisolone 40mg/day x 7-14 days, then taper

Table 4.3: Summary: Causes of Diarrhoea

Cause	Acute Diarrhoea	Chronic Diarrhoea
Bacterial Infections (watery diarrhoea, bloody, fever)	Non-typhi *Salmonella* species (NTS), *Shigella*, *Campylobacter jejuni*, *Yersinia enterocolitica*, *Escherichia coli* and *Vibrio cholera*, shigella, *Clostridium difficile*, *Vibrio cholera;* **Food borne toxigenic diarrhoea** (staph aureus, B cereus)	Salmonella typhi; Mycobacteria avium complex, mycobacterium TB
Protozoal Infections (watery diarrhoea, bloating, flatulence)	*Giardia lamblia*, *Entamoeba coli*	Cryptosporidium, *Giardia lamblia*, *Isospora belli*, Ent. histolytica, microsporidia
Parasitic		Strongyloides stercoralis
Viruses	Enteric viruses	CMV
Medication	Antibiotics, ARV drugs – PIs, DDI	ARVs
Toxins	Clostridium difficile, staph aureus, bacillus cereus	
Malignancies		Lymphoma, endocrine tumours
Other	Ischemic colitis	Endocrine disorders, malabsorption, ulcerative colitis, radiation or chemotherapy, unknown

Treatment of Toxoplasmosis

The Preferred regimen:

Pyrimethamine 200 mg loading dose, then 50 mg –75 mg/day

+

Sulfadiazine 1000 mg to 1500mg P.O. 6 hourly

+

Folinic acid (leucovorin) 10-20mg/day PO

Folate is not a substitute for Folinic acid. The dose of Folinic acid can be increased to >50 mg/day to reduce Pyrimethamine-associated haematological toxicity

Alternative regimen:

Cotrimoxazole: 5mg/kg of Trimethoprim or 25mg/kg of CTX BD per day for 6 weeks (e.g. for 60kg man, 4 SS tablets per day). This is the regimen of first choice locally in the absence of key constituents of the preferred choice above. An advantage of this regimen over the above one is that it can also be given IV in patients unable to take oral treatment.

Progress

Clinical improvement is usually expected within 1 week and improvement demonstrated by CT scan or

9.1.3. Treatment

A. When to start ART

All HIV infected patients who are co-infected with hepatitis B should be started on ART irrespective of CD4 cell count, WHO clinical stage or stage of liver disease

The general recommendations for treatment preparation, adherence counselling and support and monitoring of therapy for PLHIV apply. However, because HBV positive patients are at higher risk of hepatotoxicity, closer monitoring of liver function (with ALT) is advised. Table 9.2 provides a summary of areas of focus during initial evaluation for HIV/HBV co-infected patients initiating therapy.

B. Recommended first-line ART in HIV/HBV co-infection

The recommended first-line ART in adolescents and adults with HIV/HBV co-infection is TDF + 3TC + DTG (or TDF + 3TC + EFV for women and adolescent girls of childbearing potential)

Treatment with both TDF and 3TC is recommended as 3TC alone will result in rapid emergence of resistance. In case of renal impairment (as assessed by creatinine clearance), the dose of TDF and 3TC should be adjusted (refer to Table 9.3).

HBV And HIV

Table 9.2: Summary of Initial Clinical and Laboratory Evaluation in HIV/HBV Co-infection

	Findings	Action
History	Alcohol use, cigarette smoking, intravenous drug use, risky sexual practices, anorexia, right upper quadrant pain, jaundice, early satiety, haematemesis, dark stool, bleeding, pruritus	Assess, counsel and support to stop taking alcohol; counsel and support smoking cessation; counsel and provide or refer for harm reduction interventions
Physical examination	Enlarged liver, enlarged spleen, ascites, scratch marks	Evidence of established chronic liver disease, closer follow-up due to increased risk of hepatotoxicity, discuss or refer to a consultant for additional evaluation and management
ALT	If elevated, may point to active liver disease. Exclude other causes of elevation of liver enzymes	Every effort should be made to assess for liver function (albumin and INR), especially in symptomatic patients. However, this should not delay initiation of ART
Creatinine	Calculate creatinine clearance	In HIV/HBV co-infection, TDF is indicated even in patients with CrCl < 50 ml/min. In such patients, avoid FDCs. Instead administer the ART as single drugs to allow for dosage adjustment as shown in Table 9.3
Comorbidities	HCV antibody, random blood sugar, lipid profile, alcoholic and non-alcoholic liver disease, hepatocellular carcinoma (family history)	Refer the patient for additional investigations where these are suspected

D. Stopping treatment, treatment interruptions

TDF-containing ART should not be stopped in a patient with HIV/HBV co-infection as this may result in a flare-up of the hepatitis. If the regimen must be stopped and another alternative for suppressing hepatitis B cannot be found, liver enzymes should be monitored and treatment re-instated as soon as possible.

E. Second line for HIV/ HBV co-infected

Maintain TDF + 3TC in the ART regimen for patients switching from TDF-based-therapy.

The recommended second-line ART regimen in HIV/HBV co-infection is TDF + 3TC + ATV/r

HIV/HBV co-infected patients failing second-line ART should be discussed in the MDT and discussed with the Regional or National HIV Clinical TWG (Uliza Toll-free Hotline 0800 72 48 48; ulizanascop@gmail.com).

9.2.3. Treatment of HIV/HCV Co-infection

Table 9.4: Summary of Initial Clinical and Laboratory Evaluation in HIV/HCV Co-infection

	Findings	Action
History	Alcohol use, cigarette smoking, intravenous drug use, risky sexual practices, anorexia, right upper quadrant pain, jaundice, early satiety, haematemesis, dark stool, bleeding, pruritus	Assess, counsel and support to stop taking alcohol, counsel and support smoking cessation; counsel provide and refer for harm reduction interventions
Physical examination	Enlarged liver, enlarged spleen, ascites, scratch marks	Evidence of established chronic liver disease, closer follow-up due to increased risk of hepatotoxicity, discuss or refer to a consultant for additional evaluation and management
HCV RNA PCR	For confirmation of chronic HCV infection	If available, at baseline
HCV genotype		Important for selecting appropriate DAA regimen
ALT	If elevated, may point to active liver disease. Exclude other causes of elevation of liver enzymes	Every effort should be made to assess for liver function (albumin and INR), especially in symptomatic patients. However, this should not delay initiation of ART
Comorbidities	HBV, random blood sugar, lipid profile, alcoholic and non-alcoholic liver disease, hepatocellular carcinoma (family history)	Refer the patient for additional investigations where these are suspected

Table 9.5: Recommended DAA for the Treatment of HCV without Cirrhosis

Genotype	DAA Regimen*	Duration of treatment	ART considerations
1, 2 & 3	Daclatasvir (60 mg) + Sofosbuvir (400 mg)	12 weeks**	If the ART regimen contains EFV, increase the dose of Daclatasvir to 90 mg once daily. When used concomitantly with boosted Atazanavir, the dose of Daclatasvir should be reduced to 30 mg once daily
4	Elbasvir (50 mg + Grazoprevir (100 mg)	12 weeks	Use with ARVs with minimal interactions: TDF, ABC, 3TC, FTC, RAL and DTG
5 & 6	Ledipasvir (90 mg) + Sofosbuvir (400 mg)	12 weeks	Avoid concomitant use of TDF and Ledipasvir if the CrCl is < 50 ml/min

* Start DAA HCV therapy under specialist supervision
**Treatment duration is extended to 16 - 24 weeks in patients with compensated cirrhosis

Table 1.6: Clinical Presentation of IRIS

Responsible Condition	Clinical Presentation of IRIS
TB	IRIS presents from 1-6 wks after starting ART. Commonly high fever, cough, dyspnoea; new or increased lymphadenopathy (peripheral or mediastinal); lymph node abscesses; worsening of pulmonary disease with new or increased infiltrates or effusion; new or worsening CNS presentation; other new extrapulmonary lesions
Herpes Zoster	Within the first 4 months of ART. Presents with herpes zoster,
Cryptococcus	Presents 1 wk to 11 months after ART initiation. Fever, worsening headache, lymphadenitis, new or worsening signs of meningitis; pulmonary disease; skin lesions,
PCP	Fever, cough, dyspnoea in patients on treatment, those recently treated or those undiagnosed. CXR may show worsening radiographic picture
Skin	New or worsening PPE, eosinophilic folliculitis, new presentation or chronic mucocutaneous herpes lesions
Malignancies	New or worsening KS lesions
Hepatitis B	Worsening hepatitis, confirmed by rising ALT AST. Can present late, up to 9 months after ART initiation. "May be associated with re-appearance of positive HBSAG and HBeAG in patients previously positive HBc Ab/HBsAb"

Treatment

No single treatment option exists for IRIS and management depends on the underlying condition, as well

Immune Reconstitution Inflammatory Syndrome (IRIS)

Definition:

IRIS is a paradoxical inflammatory reaction against a foreign antigen (alive or dead) in patients who have started ART with reconstitution (improved functioning) of their immune system. The immune system, once it regains some function, is now able to respond against the foreign antigen.

Classification:

- **Unmasked IRIS:** appearance of a previously undiagnosed opportunistic infection (OI) following ART initiation (or switch of ART to a suppressive regimen)
- **Paradoxical IRIS:** worsening of a previously diagnosed disease after ART initiation (or switch of ART to a suppressive regimen)

Risk Factors for IRIS:

- 10-20% of patients who start ART with advanced immunosuppression (refer to section 3) experience clinical deterioration during the first few months due to IRIS
- High risk patients include:
    - Advanced immunosuppression (WHO Stage 3 or 4, or CD4 count ≤ 200 cell/mm3 (or CD4% ≤ 25% for children ≤ 5 years old))
    - Patients with a diagnosed opportunistic infection like TB, MAC, CMV, and PCP
    - Low baseline CD4 (CD4 count ≤ 50 cell/mm³ or CD4% ≤ 10%)
    - High baseline viral load
    - Substantial increase is CD4 count and drop in viral load after starting ART

Diagnosis of IRIS

- IRIS should be suspected any time a patient has clinical deterioration weeks to months after starting ART (or switching to a suppressive ART regimen)
- Clinical deterioration usually occurs within 4-8 weeks of initiation or change of ART (but can be months afterwards)
- IRIS has varied clinical presentations due to multiple possible pathogens that the immune system may be reacting to, and various immune system reactions; there are generally clinical manifestations consistent with an inflammatory condition
- A high level of suspicion is required when making a diagnosis of IRIS, which is generally one of exclusion
- Rule out the possibility of drug reaction, patient non-adherence to OI treatment, persistently active infection and/or drug resistance to OI treatment
- There could be localized tissue inflammation with or without systemic inflammatory response

Patient evaluation:

In addition to the clinical evaluation for PLHIV outlined in Table 3.1, emphasis should be placed on the following areas during the patient evaluation:

History:

Symptoms and current ARV history:

- Specific systemic symptomatology
- Date of ARV initiation
- Regimen
- Reason for substitution / switch from previous ART if not first line
- Adherence to ART and other ongoing treatment
- HIV viral load
- CD4 count

Prior History:	**History of treatment of opportunistic infections:**
• ARV toxicity • Drug-drug interaction • CD4 count • HIV viral load	• Date of initiation of treatment • Duration of therapy • Clinical response to treatment • Adherence to the OI treatment • Any default to treatment • Resistance to treatment

Physical Examination:

Vital signs assessment: Temperature, Heart Rate, Blood Pressure, Respiratory rate

Conduct a detailed systemic examination:

- Emphasis should be placed on the system(s) which are primarily affected (Table 3.1)

Investigations

- All patients with advanced HIV disease should be screened for common OIs including TB, cryptococcal meningitis and other common OIs depending of their presenting signs and symptoms

Major and Minor Presentations of IRIS

Major presentation	Minor presentation
Tuberculosis (TB) Mycobacterium avium complex (MAC) Cryptococcal meningitis Cytomegalovirus (CMV) retinitis Hepatitis B or C virus Progressive multifocal leukoencephalopathy (PML) Kaposi's sarcoma Cerebral toxoplasmosis Autoimmune diseases	Herpes simplex virus (HSV) and varicella zoster virus (VZV) Nonspecific dermatologic complications such as folliculitis and oral and genital warts

Management of IRIS

IRIS management is dependent on severity of symptoms and the following general guidance is recommended:

Severity of IRIS	Definition	Management

Mild	• Resolves over time in most patients
	• Symptomatic treatment is often sufficient
		• Treat the OI and manage the associated symptoms
		• Treat IRIS-associated inflammation:
		  ○ NSAIDS for discomfort associated with mild inflammation / fevers
		  ○ Inhaled steroids for bronchospasm or cough associated with mild pulmonary inflammation
		• Surgical intervention:
		  ○ Drainage of abscesses
		  ○ Excision of inflamed and painful lymph nodes

Severe	• Threatens a patient's functional state
	• Cause permanent disability
	• Potentially lead to death
	Examples:
	• Decline in pulmonary capacity from TB or MAC infection
	• Neurologic complications from cryptococcal infection
	• Loss of vision from CMV retinitis infection
		• Treat the OI and manage the associated symptoms
		• Manage the IRIS-associated inflammation:
		  ○ If NOT cryptococcal meningitis or KS: give 1 to 2 mg/kg prednisone for 1 to 2 weeks. Follow with a period of individualized tapering of the dose
		  ○ Do not use corticosteroids for the management of CM or KS- related IRIS
		• Closely monitor patients on corticosteroid therapy for:
		  ○ Hyperglycemia
		  ○ Hypertension
		  ○ Mental status changes
		  ○ Avascular necrosis
		  ○ Worsening of an existing infection
		  ○ Predisposition to a new infection (e.g. TB and CMV)