WESTERN CAPE ART GUIDELINES 2019

ADOLESCENTS (≥ 10 YEARS) AND ADULTS

First edition December 2019

NEED HELP?

Contact the TOLL-FREE National HIV & TB Health Care Worker Hotline

0800 212 506 / 021 406 6782

Alternatively "WhatsApp" or send an SMS or "Please Call Me" to 071 840 1572

www.mic.uct.ac.za

ART ELIGIBILITY AND DETERMINING THE TIMEFRAME FOR ART INITIATION

WHO IS ELIGIBLE?

All people living with HIV (PLHIV) regardless of age, CD4 cell count and clinical stage. ART should be initiated within 7 days unless there is a reason to defer. Same day initiation is encouraged if patient is clinically well and motivated

REASONS TO DEFER STARTING ART	WHEN TO START ART*
TB symptoms (cough, night sweats, fever, recent weight loss)	No TB: Same day or within 7 days Confirmed DS-TB at non-neurological site: CD4 < 50 cells/μL: within 2 weeks of starting TB treatment CD4 ≥ 50 cells/μL: 8 weeks after starting TB treatment Confirmed DR-TB at non-neurological site: Start ART 2 weeks after TB treatment, once symptoms improved and TB treatment tolerated
Signs and symptoms of meningitis (headache, confusion, fever, neck stiffness or coma)	Investigate for meningitis before starting ART TBM (DS or DR): 4-8 weeks after starting TB treatment CM: 4-6 weeks after starting antifungal treatment
CrAg-positive with no symptoms or signs of meningitis	2 weeks after starting fluconazole
Other acute illnesses e.g. PJP or bacterial pneumonia	Defer ART for 1-2 weeks after commencing treatment for the infection
Clinical symptoms or signs of liver disease	Confirm liver disease using ALT and bilirubin. ALT > 120 IU/L with symptoms of hepatitis (nausea, vomiting, upper quadrant pain) and/or total serum bilirubin concentrations > 40 μmol/L: investigate and manage possible causes before starting ART

*Clients already on ART should NOT have their treatment interrupted upon diagnosis of the above conditions

BASELINE CLINICAL INVESTIGATIONS

- Recognise the client with respiratory, neurological, or abdominal danger signs
- Nutritional assessment
- TB symptomatic screening. (If pregnant do GeneXpert regardless of symptoms)
- Meningitis symptomatic screen (headache, confusion, fever, neck stiffness or coma)
- Mental health issues/substance abuse
- Major chronic non-communicable diseases (NCDs) e.g. diabetes, hypertension, epilepsy
- Pregnancy or planning to conceive
- Symptom screen for sexually transmitted infections (STIs)
- WHO clinical stage
- Weight and height in adolescents and adults

BASELINE LABORATORY EVALUATION

TEST AND PURPOSE	INTERPRETATION / ACTION
Confirm HIV test result To confirm HIV status for those without documented HIV status	Ensure that the national testing algorithm has been followed
CD4 count (cells/μL) To identify eligibility for CPT and CrAg screening	Initiate CPT if CD4 < 200 or WHO stage 2, 3 or 4 If **CD4 < 100** a reflex CrAg screening will be done automatically **CrAg-negative:** no fluconazole therapy required. Start ART **CrAg-positive and asymptomatic:** start fluconazole therapy, unless patient is pregnant. If pregnant, refer for LP. Start ART after 2 weeks **CrAg-positive and symptomatic (symptoms include: headache, confusion):** refer for LP and start antifungal treatment as per CM guidelines. Defer ART as above
Cervical cancer screening To identify women with cervical lesions	At baseline and thereafter every three years if normal. If lesions present, refer for colposcopy and manage accordingly
Creatinine and eGFR To detect renal insufficiency, and eligibility for TDF	Serum creatinine (SCr) is a waste product filtered by the kidneys used to determine eGFR

Age/Pregnancy status	What must be measured?	Safe to use TDF
≥ 10 and < 16 years	eGFR using Counahan Barratt formula[#]	> 80 mL/min/1.73 m^2
Adult and adolescent ≥ 16 years	eGFR using MDRD equation as provided by the laboratory	> 50 mL/min/1.73m^2
Pregnant	Absolute creatinine level	< 85 μmol/L

[#]**Counahan Barratt formula**

eGFR (mL/min/1.73 m^2) = height [cm] x 40 / creatinine [μmol/L]

	Adults and adolescents	Pregnant women
FBC and differential WCC To detect anaemia and neutropenia	If Hb < 10 then follow Primary Care Standard Treatment guidelines If Hb < 8 avoid AZT	If Hb < 10 initiate iron supplementation Refer if: Hb < 8 with symptoms of anaemia, or anaemia and ≥ 36 weeks pregnant, or no response to iron *Take note of DTG drug interactions under key points*
GeneXpert To diagnose TB	Do GeneXpert only if patient has symptoms of TB. Send 2 sputum samples	Routinely done at first antenatal visit, regardless of symptoms

3TC = lamivudine; **ABC** = abacavir; **ART** = antiretroviral therapy; **ATV/r** = atazanavir and ritonavir; **AZT** = zidovudine; **CM** = Cryptococcal meningitis; **CPT** = cotrimoxazole preventive therapy; **CrAg** = cryptococcal antigen; **DR** = drug-resistant; **DS** = drug-sensitive; **DTG** = dolutegravir; **DRV/r** = darunavir and ritonavir; **EFV** = efavirenz; **eGFR** = estimated glomerular filtration rate; **FBC** = full blood count; **FTC** = emtricitabine; **HBV** = hepatitis B virus; **HBsAg** = hepatitis B surface antigen; **InSTI** = Integrase strand transfer inhibitor; **LPV/r** = lopinavir and ritonavir; **LP** = lumbar puncture; **NNRTI** = non-nucleoside reverse transcriptase inhibitor; **NVP** = nevirapine; **PI** = protease inhibitor; **OI** = opportunistic infection; **PJP** = *Pneumocystis jirovecii* pneumonia; **TB** = Tuberculosis; **TBM** = Tuberculosis meningitis; **TDF** = tenofovir; **TLD** = tenofovir + lamivudine + dolutegravir; **TEE** = tenofovir + emtricitabine + efavirenz; **TC** = total cholesterol; **TG** = triglycerides; **VL** = viral load; **WCC** = white cell count

REGIMENS

RECOMMENDED FIRST-LINE IN NEW PATIENTS

Adult women and adolescent girls ≥ 35 kg and ≥ 10 years Provide information on risks and benefits of TEE and TLD to allow client to make an informed choice. Document that woman has been counselled and consents to receive DTG	Not pregnant	Not childbearing potential	TLD
		Childbearing potential, not planning to fall pregnant, offer contraception	TLD
		Childbearing potential, wanting to conceive	TEE
	Pregnant	First 6 weeks of gestation	TEE
		After 6 weeks gestation	TLD
Adult men and adolescent boys ≥ 35 kg and ≥ 10 years of age			TLD
Client currently on DS-TB treatment at ART initiation			TEE

SWITCHING PATIENTS WHO ARE STABLE ON A FIRST-LINE REGIMEN TO DOLUTEGRAVIR

Latest VL (copies/mL) result (within the past 6 months):

If VL not done within the past 6 months, wait for next routine VL

Only switch a **stable pregnant woman** on ART from EFV to DTG if her VL is < 50 copies/mL, and she **is more than 6 weeks pregnant**

VL < 50	Discuss benefits and risks of switching[¤] and the use of contraception in women of childbearing potential. **If patient chooses to switch to DTG:**	
	Current regimen:	**New regimen:**
	TDF + (FTC or 3TC) + (EFV or NVP)	TLD
	(AZT or ABC)[¥] + 3TC + (EFV or NVP)	(AZT or ABC) + 3TC + DTG
VL ≥ 50	Do not switch. Refer to section on viral load monitoring. If the repeat VL after 3 months is between 50— 999, discuss patient with an expert	

[¤]Assess the reason for exclusion of TDF from the NRTI backbone. If TDF was excluded due to TDF-induced nephrotoxicity, continue using the same NRTI backbone. If TDF was excluded due to non-TDF related renal failure that has since resolved, then the use of TDF can be reconsidered. Before switching to TDF, ensure adequate renal function by checking eGFR/creatinine as outlined in the Baseline Laboratory Evaluation Table

SECOND- AND THIRD-LINE REGIMENS WITH CONFIRMED VIROLOGICAL FAILURE

	FIRST-LINE REGIMENS				SECOND-LINE REGIMENS	
REGIMEN	NNRTI-based Regimen		InSTI-based Regimen for > 2 years		PI-based Regimen for > 2 years	
	TDF + 3TC/FTC + **EFV/NVP**		**TDF** + 3TC/FTC + **DTG**		**AZT/TDF** + 3TC/FTC + **LPV/r or ATV/r**	
RESISTANCE TESTING	Resistance test **not** required		Resistance testing may be required under expert consultation		Resistance test required	
RESISTANCE TEST RESULTS	Not applicable		Not applicable		No PI resistance	PI resistance
HBV CO-INFECTION	HBV-negative	HBV-positive	HBV-negative	HBV-positive	HBV-positive[#] or - negative	
NEW REGIMEN	AZT + 3TC + DTG If DTG not suitable: AZT + 3TC + LPV/r	TDF + AZT + 3TC/ FTC + DTG If DTG not suitable: TDF + 3TC + LPV/r	AZT + 3TC + LPV/r	TDF + 3TC/ FTC + LPV/r	Continue current regimen and address adherence or discuss PI substitution with an expert	Refer to third-line committee. Regimen will be determined by results of resistance test

Ideally patients who are HBsAg-positive should be on a TDF-based regimen if feasible

KEY POINTS ON THE USE OF DTG vs EFV

	DOLUTEGRAVIR	EFAVIRENZ
Resistance	• Provides rapid viral suppression • High genetic barrier to resistance	• Low genetic barrier to resistance
Side-effects	• Side-effects are mild and uncommon • Weight gain • Insomnia	• Neuropsychiatric side-effects
Interactions[ϖ]	• Drug interactions with rifampicin, metformin, some anti-convulsants and polyvalent cations (Mg^{2+}, Fe^{2+}, Ca^{2+}, Al^{3+}, Zn^{2+}) • No interaction with hormonal contraceptives	• No significant interaction with rifampicin • Drug interactions with hormonal contraceptives, and many other medicines metabolised by the liver
Pregnancy	• DTG may increase the risk of neural tube defects (NTDs) if used in the first six weeks of pregnancy	• Safe in pregnancy

[ϖ]For more information on drug-drug interactions contact the National HIV- & TB HCW hotline at 0800 212 506

FOLLOW-UP MONITORING IN PATIENTS ON ART

CLINICAL ASSESSMENT AND RESPONSE

- Weight
- WHO clinical staging
- Screen for TB and other OIs
- Screen for pregnancy and ask if planning to conceive
- Ask about side effects, especially sleep and gastrointestinal disturbances

VIROLOGICAL AND IMMUNOLOGICAL RESPONSE TO ART

TEST	ACTION/INTERPRETATION
CD4 count At 1 year on ART	Repeat CD4 6 monthly **only** if CD4 < 200 **or** VL ≥ 50 on two consecutive occasions Stop CD4 monitoring if VL < 1000 and CD4 > 200. Stop CPT if CD4 > 200
Viral Load (VL) Clients on first line: Month 4, 12 and then 12-monthly if virologically suppressed Clients on second or third line: Month 6, 12 and then 12-monthly if virologically suppressed If DR-TB: every 6 months until DR-TB treatment completed	

VL	RESPONSE
≥ 1000	Do thorough assessment of the cause of an elevated VL: Consider adherence problems, intercurrent infections, incorrect ART dose, drug interactions and resistance. Implement interventions, including adherence support. Do HBsAg if not done previously and currently on TDF-based treatment. Repeat VL in 3 months (2 months after adherence intervention) If VL still ≥ 1000 and on **NNRTI-based** regimen: Consider switching to second-line if virological failure confirmed, i.e. VL ≥ 1000 on 2 consecutive occasions and adherence issues addressed If VL still ≥ 1000 and on **PI- or InSTI (DTG)-based** regimen: Consider resistance test if virological failure confirmed, i.e. VL ≥ 1000 on at least 3 occasions over the course of 2 years, or VL ≥ 1000 with signs of immunological or clinical failure (i.e. declining CD4 and/or opportunistic infections) Do genotype resistance testing if no dose adjustments were made while on a PI or DTG to overcome significant drug interactions e.g. rifampicin
50 – 999	Do thorough assessment of the cause of an elevated VL. Consider adherence problems, intercurrent infections, incorrect ART dose, drug interactions and resistance. Implement interventions, including adherence support. Repeat VL after 3 months. If VL 50 - 999 again, repeat in 6 months. For VL < 50 or ≥ 1000 follow table
< 50	Continue routine VL monitoring and routine adherence support. Patient is doing well

LABORATORY MONITORING WHILE ON ART

DRUG	TEST	FREQUENCY	ACTION/INTERPRETATION
TDF	Creatinine	Month 1, 4 and 12. Then 12-monthly	See creatinine and eGFR section at baseline laboratory testing
AZT	FBC + differential WCC	Month 1, 3 and 6, thereafter if clinically indicated	Hb > 8 g/dL: Continue AZT Hb ≤ 8 g/dL: Use alternative – consult with expert
PI-based regimen (LPV/r, ATV/r, DRV/r)	Cholesterol + triglycerides (TGs)	At month 3. Repeat annually if clinically indicated	To monitor LPV/r- related metabolic side-effects. If total cholesterol > 6mmol/L, consider switch to ATV/r. Management of hyperlipidaemia should include dietary modification. Refer if TG > 10 mmol/L
TB treatment **or** NVP **or** EFV	ALT	Signs/symptoms of hepatitis (e.g. nausea, vomiting, jaundice)	If ALT is abnormal, refer to specialist or phone the HIV hotline (0800 212 506)

DOSAGE

ANTIRETROVIRAL	USUAL ADULT DOSE	DOSE ADJUSTMENT IN RENAL IMPAIRMENT	
		eGFR 10 - 50 mL/min	eGFR < 10 mL/min
Abacavir (ABC)	300 mg twice daily OR 600 mg once daily	Normal dose	Normal dose
Atazanavir + ritonavir (ATV/r)	300 mg/100 mg once daily	Normal dose	Normal dose
Darunavir + ritonavir (DRV/r)	600 mg/100 mg twice daily OR 800 mg/100mg daily (depending on mutations)	Normal dose	Normal dose
Dolutegravir (DTG)	**No integrase inhibitor mutations:** 50 mg daily. If also on rifampicin: Boosting of DTG required. The dosing frequency of DTG should be increased to 50 mg 12 hourly. If on TLD FDC, then add DTG 50 mg 12 hours after TLD. Continue boosting until 2 weeks after rifampicin discontinued **Integrase inhibitor mutations present:** 50 mg twice daily. If also on rifampicin, avoid DTG	Normal dose	Normal dose
Efavirenz (EFV) (Swallow tablet whole)	600 mg daily (or 400 mg if < 40 kg); usually given at night	Normal dose	Normal dose
Emtricitabine (FTC)	200 mg once daily (not available as single agent)	Not applicable	Not applicable
Lamivudine (3TC)	150 mg twice daily OR 300 mg once daily	150 mg daily	50 mg daily
Lopinavir + ritonavir (LPV/r) (Swallow tablet whole)	400 mg/100 mg twice daily NB: Patients on a rifampicin-containing TB regimen: Increase LPV/r to 800/200 mg twice daily slowly over 2 weeks with ALT monitoring. Continue double dose for 2 weeks after stopping rifampicin	Normal dose	Normal dose
Raltegravir (RAL)	400 mg twice daily	Normal dose	Normal dose
Tenofovir (TDF)	300 mg once daily	Avoid use	Avoid use
Zidovudine (AZT)	300 mg twice daily	Normal dose	300 mg daily

Based on the Western Cape Consolidated Guidelines for HIV Treatment: Prevention of Mother-to-Child Transmission of HIV (PMTCT), Children, Adolescents and Adults 2019.