WESTERN CAPE ART CLINICAL GUIDELINES 2023

ADOLESCENTS (≥ 10 YEARS), ADULTS, PREGNANT AND BREASTFEEDING WOMEN (PBFW)

March 2024, Version 2

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 or download our free SA HIV/TB Hotline App—scan QR code

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. For all clients without contra-indications, ART should be initiated within 7 days, and on the same day if possible. Pregnant women and clients with advanced HIV disease should be prioritised for rapid initiation. However, all clients, particularly those with advanced HIV disease, should be carefully assessed for opportunistic infections that may necessitate ART deferral (see below)

REASONS TO DEFER STARTING ART	WHEN TO INITIATE ART*
TB symptoms (cough, night sweats, fever, recent weight loss) **Think PredART to reduce the risk of IRIS. For clients with advanced HIV-disease (CD4 < 100) initiating ART with TB diagnosis within the past month. Phone the hotline for help: 0800 212 506**	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 PBFW: within 2 weeks of starting TB treatment, once symptoms improve and TB treatment is tolerated Confirmed DR-TB at non-neurological site: Initiate ART after 2 weeks of TB treatment, once symptoms improve and TB treatment is 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 PBFW: 4 - 6 weeks after starting CM or TBM (DS or DR) treatment
CrAg-positive with no symptoms or signs of meningitis and LP is negative for CM	No need to delay ART. ART can be started immediately
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

***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 (including weight and height)
- WHO clinical stage

Screen for:
– Symptoms of meningitis (i.e. headache, confusion, visual disturbances)
– Active depression, other mental health issues or substance abuse
– Major chronic non-communicable diseases (NCDs) e.g. diabetes, hypertension, epilepsy
– Pregnancy or planning to conceive
– Symptom screen for sexually transmitted infections

BASELINE LABORATORY EVALUATION

TEST AND PURPOSE	INTERPRETATION / ACTION
Confirm HIV test result For those without documented HIV status	Ensure that the national testing algorithm has been followed
CD4 count (cells/µL) Identify eligibility for CPT and CrAg screening	Initiate CPT if CD4 ≤ 200 or WHO stage 2, 3 or 4 If **CD4 < 200**, a reflex CrAg screening will be done automatically **CrAg-negative:** no fluconazole therapy required. Start ART **CrAg-positive:** the client will require treatment of the infection. Refer for LP. Defer ART
Cervical cancer screening To identify women with cervical lesions and manage appropriately	All HIV-positive women should be screened for cervical cancer at diagnosis and subsequently every 3 years if the screening test is negative. If a possible abnormality of the cervical cells is detected, develop a clear plan for further investigation and treatment. Pregnancy: cervical cancer screen can be done up to 20 weeks' gestation
Syphilis testing	For all clients initiating ART
Creatinine and eGFR To assess renal insufficiency *DTG is known to decrease tubular secretion of creatinine without affecting glomerular filtration. Serum creatinine concentrations increase early in treatment, remain stable throughout therapy, and are not an indication to stop DTG. A creatinine level that keeps on rising, is however a cause for concern and could indicate TDF toxicity or other underlying pathology*	Serum creatinine (SCr) is a waste product filtered by the kidneys; used to determine eGFR **Age/Pregnancy status** / **What must be measured?** / **May use TDF** **≥ 10 and < 16 years** / eGFR using Counahan Barratt formula[#] / > 80 mL/min/1.73m^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]
Haemoglobin (Hb) **Only for patients starting AZT** To detect and manage anaemia, to determine eligibility for AZT where necessary	**Adults and adolescents**: If Hb is low, do FBC and follow Primary Care Standard Treatment guidelines If Hb < 8 g/dL: avoid AZT **Pregnant women**: If Hb < 10 g/dL: treat with ferrous sulphate tds Refer if Hb < 8 g/dL with symptoms of anaemia, or anaemia and ≥ 36 weeks pregnant, or no response to iron *Take note of DTG interaction with polyvalent cations, e.g. iron. See the interaction checker on the hotline app—scan QR code*
TB symptom screen and TB-NAAT (e.g. GXP) and U-LAM To diagnose TB and establish eligibility for TPT	For PLHIV, regardless of symptoms, do TB-NAAT (e.g. GXP): • At time of HIV diagnosis. If TB-NAAT negative and symptom screen negative, consider TPT • On enrolment in antenatal care for pregnant women • At every 12-monthly clinical review for clients on ART (aligned with yearly VL) ***Symptomatic patients:*** TB-NAAT. If **admitted to hospital** also do U-LAM, chest X-ray if indicated and other investigations for extra-pulmonary TB if clinically indicated. Enquire about TB contacts. In the **outpatient setting** do U-LAM if CD4 < 200 within the last 6 months, or patient has advanced HIV disease or current serious illness. Do chest X-ray if clinically indicated

REGIMENS

RECOMMENDED FIRST-LINE IN NEW CLIENTS

Adults, PBFW[#], adolescents ≥ 30 kg and ≥ 10 years of age	TLD
Adult clients on TB treatment at initiation of ART	TEE[§] or TLD (see drug interactions table below)
Adolescents < 30 kg and children < 10 years	Refer to paed guidelines

[#]If client diagnosed during labour, give a stat single fixed-dose TLD and stat single dose of NVP. Start lifelong ART the following day [§]EFV should only be used in ART-naïve clients. EFV has no significant interactions with rifampicin and has the benefit of being a once-daily regimen which supports adherence

SWITCHING TO DOLUTEGRAVIR

NON VL-DEPENDENT REGIMEN SWITCHES

CURRENT REGIMEN	CRITERIA FOR SWITCH	REGIMEN IF CHANGE IS INDICATED
TEE **or** ABC+3TC+(EFV or NVP) **or** AZT+3TC+(EFV or NVP) **or** TDF+3TC/FTC+NVP **or** AZT+3TC+DTG **or** Any LPV/r or ATV/r regimen for < 2 years	**Switch all, regardless of VL** Review VL in last 12 months: **VL < 50:** continue normal VL monitoring **VL ≥ 50:** switch, but do ABCDE assessment, provide EAC (if needed) **VL not done in last 12 months:** switch, and do VL on same day. Don't wait for result before switching	No renal dysfunction, ≥ 10 years of age and weight ≥ 30 kg: **TLD** If client does not qualify for TDF: **ABC + 3TC + DTG** If client doesn't qualify for TDF and has ABC hypersensitivity: **AZT + 3TC + DTG**

VL-DEPENDENT REGIMEN SWITCHES

Clients on PI-based regimens > two years, who have never used a DTG-containing regimen in the past: switch to DTG is based on their VL within the last 12 months

VL (c/mL) (within the last 12 months)	CURRENT REGIMEN	CRITERIA FOR SWITCH	REGIMEN IF CHANGE IS INDICATED
VL < 1000[**]	LPV/r or ATV/r based regimen > 2 years	**Switch to DTG-containing regimen** If VL in last 12 months ≥ 50: switch, but do ABCDE assessment and provide EAC if needed. Repeat VL after 3 months	No renal dysfunction, ≥ 10 years of age and weight ≥ 30 kg: **TLD** If client does not qualify for TDF: **ABC + 3TC + DTG** If client doesn't qualify for TDF and has ABC hypersensitivity: **AZT + 3TC + DTG**
Two or more consecutive VLs ≥ 1000 taken ≥ 2 years after starting LPV/r or ATV/r regimen	Adherence < 80 %	**Switch to DTG-containing regimen. Do not do resistance test**	
	Adherence > 80 %	**These clients do not qualify for a same day switch.** Discuss with an HIV expert or the hotline (0800 212 506) to authorise and interpret a resistance test. Provide individualised regimen as recommended by HIV expert. Repeat VL after 3 months to confirm re-suppression	
Only one VL > 1000 after 2 years on a LPV/r or ATV/r regimen[##]	Do ABCDE assessment, EAC if applicable, repeat VL after 3 months. This result will group the client into one of the above categories		

[**]Patients virologically suppressed on 2nd line ART with a boosted PI can be retained on their regimen until existing PI stocks are depleted; [##] Resistance testing might be indicated if there is evidence of clinical and/or immunological failure with good adherence—discuss with an expert or call the hotline

Remember to do the HBsAg when considering switch from a TDF-containing regimen to non-TDF containing regimen

HOW TO OBJECTIVELY MEASURE ADHERENCE

For adherence to be > 80 %, patient must meet **one** of the following criteria:
- Pharmacy refills > 80 % in the last 6 - 12 months
- Attendance of > 80% of scheduled clinic visits in the last 6 - 12 months

To calculate adherence percentage in the past 6 - 12 months:

$$\frac{\text{Amount of scheduled visits actually attended by client}}{\text{Amount of scheduled visits}} \times 100$$

IMPORTANT DRUG INTERACTIONS BETWEEN ARVS AND TB MEDICINES[Φ]

INTERACTING MEDICINES	INTERACTION	MANAGEMENT
Rifampicin and DTG	Rifampicin decreases DTG levels	Increase DTG dose to 50 mg **twice** daily
Rifampicin and ATV/r or DRV/r	Rifampicin decreases ATV and DRV levels. Increases ALT/AST	Avoid concurrent use with ATV/r and DRV/r as dose adjustment not established. Consider rifabutin 150 mg daily as an alternative to rifampicin
Rifampicin and LPV/r	Rifampicin decreases LPV levels. Increases ALT/AST	The dose of LPV/r should be doubled slowly over 2 weeks (to 800/200 mg twice daily). Monitor ALT while increasing the dose at weekly intervals, and then monthly while on double dose
Bedaquiline (BDQ) and EFV	EFV decreases BDQ levels. Also additive risk of QT prolongation	Avoid combination. Phone the hotline to discuss switching EFV to DTG or LPV/r
Linezolid and AZT	Additive mitochondrial and haematotoxicity	Linezolid and AZT should not be used together

[Φ]This list is not exhaustive. Download the free SA HIV/TB Hotline app for a complete interaction checker – scan QR code in the NEED HELP box

If patient comes from a different facility, provide patient with treatment on the day of presentation. Referral letters are helpful, however a patient shouldn't be required to leave the facility without treatment to first obtain a referral/transfer letter

MONITORING WHILE ON ART

When monitoring ART, integrate monitoring for other chronic conditions, e.g. hypertension, diabetes and mental health

VL monitoring on first line: Month 4, then month 12, then annually

Creatinine and eGFR: Month 1, 4, 12 then annually

Hb if on AZT: Month 3. Repeat FBC and diff if clinically indicated

Cholesterol and triglycerides: At month 3 after starting PI-based treatment

TB-NAAT (e.g. GXP): yearly, regardless of symptoms

CD4: at baseline (then see below)

At every visit:
- Review laboratory results. If eGFR < 50, phone the hotline (0800 212 506) to discuss changing ART. If VL ≥ 50, see table on VL monitoring. If CD4 < 200, see table on CD4 monitoring
- Counselling (travel plans, VL education)
- Integrated services for family planning and NCDs
- Do clinical assessment - weight; screen for TB and other OIs; WHO staging; pregnancy and discuss plans to conceive
- Ask about side effects

CD4 MONITORING

CD4 > 200	Repeat once at month 12 (align with VL)
CD4 ≤ 200	Repeat at month 12, and then 6-monthly until CD4 > 200. Stop CD4 monitoring if client's VL remains < 1000

Other scenarios to do CD4:
- If VL > 1000: repeat CD4 6-monthly until VL < 1000
- A clinical indication arises, such as WHO Stage 3 or 4 in previously well client
- Client missed appointment > 90 days: do CD4

RESPONSE TO VL WHILE ON DTG-CONTAINING REGIMEN

RESPONSE TO VL RESULT

< 50: Continue yearly monitoring

≥ 50: Do thorough assessment of the cause of an elevated VL: Consider adherence problems, intercurrent infections, incorrect ART dose, drug interactions and resistance (if on treatment for > 2 years). Implement interventions, including EAC. Do HBsAg if not done previously and currently on TDF-based treatment. Recommend condom use and contraception, as appropriate. Repeat VL after 3 months and follow recommendations below. Also see section on CD4 monitoring

REPEAT VL RESULT

< 50: Continue yearly monitoring
≥ 50: Re-assess and resolve adherence issues urgently and see below

< 2 years	≥ 2 years		
	Adherence < 80 % or persistent low-level viraemia (2 or more consecutive VLs between 50 and 999)	**Adherence > 80 %, and with 2 or more VLs ≥ 1000 taken ≥ 2 years after starting TLD regimen OR at least one VL ≥ 1000 and either CD4 < 200 or an opportunistic infection**	
		TLD 1[#] **Clients who have never failed a previous ART regimen**	**TLD 2** **Clients who have failed a previous ART regimen**
• Intensify efforts to resolve adherence issues • Repeat VL at next scheduled routine VL	• Intensify adherence (ABCDE) • Repeat VL at next scheduled routine VL	• Intensify adherence (ABCDE) • Repeat VL at next scheduled routine VL Do RT after discussion with TLART only: • If client was incorrectly classified as TLD1 (including perinatally infected adolescents); or • Relevant drug interactions	• Discuss with an HIV expert to authorise and interpret RT • Do VL 3 months after new regimen implemented

[#]Resistance to a first-line DTG-containing regimen is extremely rare. Suboptimal adherence remains the most probable cause for non-suppression. Most clients will re-suppress on DTG-containing regimen if adherent

Indications for resistance testing:
- PI based regimen or TLD2/ALD2 for > 2 years with virological non-suppression defined as at least TWO viral load measurements of ≥ 1000 c/mL taken 2 years after starting the regimen OR 1 viral load >1000 c/mL with evidence of clinical and/or immunological failure with objective measurement of good adherence
- PI or InSTi based regimen for <2 years with virological non-suppression and a history of non-boosting of a PI-based regimen or no dose adjustment of dolutegravir to overcome a drug interaction

Note: InSTi resistance on TLD1/ALD1 is considered to be very uncommon- resistance testing is not recommended except in special circumstances: incorrect classification of TLD1 (including perinatally infected adolescents; or relevant drug-drug interactions). All applications for resistance testing and third line should be submitted to the WC Third line committee.

3TC=lamivudine; **ABC**=abacavir; **ALD**=abacavir + lamivudine + dolutegravir; **ALT**=alanine transaminase; **ART**=antiretroviral therapy; **AST**=aspartate transaminase; **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; **EAC**=enhanced adherence counselling; **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; **NCD**=non-communicable disease; **NRTI**=enucleoside reverse transcriptase inhibitor; **NNRTI**= non-nucleoside reverse transcriptase inhibitor; **NVP**=nevirapine; **PBFW**=pregnant and breastfeeding woman; **Paed**=paediatric; **PI**=protease inhibitor; **OI**=opportunistic infection; **PJP**= *Pneumocystis jirovecii* pneumonia; **RPC**=repeat prescription collection; **RT**=resistance test; **TB**=Tuberculosis; **TBM**=Tuberculosis meningitis; **TB-NAAT**=TB Nucleic acid amplification test; **TDF**=tenofovir; **tds**=three times daily; **TLART**=third line antiretroviral therapy; **TLD**=tenofovir + lamivudine + dolutegravir; **TLD1/ALD1**=clients on a DTG-containing regimen, who have never failed any other regimen (previous "first-line" terminology); **TLD2/ALD2**=clients on a DTG-containing regimen, who have failed any other regimen; **TEE**=tenofovir + emtricitabine + efavirenz; **TG**=triglycerides; **TPT**=TB preventive therapy; **VL**=viral load; **WCC**=white cell count

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