# SOUTH AFRICAN ART CLINICAL GUIDELINES 2023

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

October 2023, Version 4

## 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<br>(cough, night sweats, fever, recent weight loss) | No TB: same day or within 7 days<br>Confirmed DS-TB at non-neurological site:<br>CD4 < 50 cells/µL: within 2 weeks of starting TB treatment<br>CD4 ≥ 50 cells/µL: 8 weeks after starting TB treatment<br>PBFW: within 2 weeks of starting TB treatment, once symptoms improve and TB treatment is tolerated<br>Confirmed DR-TB at non-neurological site:<br>Initiate ART after 2 weeks of TB treatment, once symptoms improve and TB treatment is tolerated |
| Signs and symptoms of meningitis<br>(headache, confusion, fever, neck stiffness or coma) | Investigate for meningitis before starting ART<br>TBM (DS or DR): 4 - 8 weeks after starting TB treatment<br>CM: 4 - 6 weeks after starting antifungal treatment<br>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.<br>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**<br>For those without documented HIV status | Ensure that the national testing algorithm has been followed |
| **CD4 count (cells/µL)**<br>Identify eligibility for CPT and CrAg screening | Initiate CPT if CD4 ≤ 200 or WHO stage 2, 3 or 4<br>If **CD4 < 100**, a reflex CrAg screening will be done automatically<br>**CrAg-negative:** no fluconazole therapy required. Start ART<br>**CrAg-positive:** the client will require treatment of the infection. Refer for LP. Defer ART |
| **Cervical cancer screening**<br>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 |
| **HBsAg**<br>Identify hepatitis B co-infection | If positive, TDF-containing regimen is preferred. Exercise caution when stopping TDF due to risk of hepatitis flares |
| **Creatinine and eGFR**<br>To assess renal insufficiency<br>*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<br>**Age/Pregnancy status** / **What must be measured?** / **May use TDF**<br>**≥ 10 and < 16 years** / eGFR using Counahan Barratt formula[#] / > 80 mL/min/1.73 m$^2$<br>**Adult and adolescent ≥ 16 years** / eGFR using MDRD equation as provided by the laboratory / > 50 mL/min/1.73m$^2$<br>**Pregnant** / **Absolute** creatinine level / < 85 µmol/L<br>**[#]Counahan Barratt formula**<br>eGFR (mL/min/1.73 m$^2$) = height [cm] x 40 / creatinine [µmol/L] |
| **Haemoglobin (Hb)**<br>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<br>If Hb < 8 g/dL: avoid AZT<br>**Pregnant women**: If Hb < 10 g/dL: treat with ferrous sulphate tds<br>Refer if Hb < 8 g/dL with symptoms of anaemia, or anaemia and ≥ 36 weeks pregnant, or no response to iron<br>*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 MTB/Rif Ultra (Xpert) and U-LAM**<br>To diagnose TB and establish eligibility for TPT | For PLHIV, regardless of symptoms, do GXP:<br>• At time of HIV diagnosis. If GXP negative and symptom screen negative, consider TPT<br>• On enrolment in antenatal care for pregnant women<br>• At every 12-monthly clinical review for clients on ART (aligned with yearly VL)<br>***Symptomatic patients:*** MTB/Rif Ultra (Xpert). 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**<br>ABC+3TC+(EFV or NVP) **or**<br>AZT+3TC+(EFV or NVP) **or**<br>TDF+3TC/FTC+NVP **or**<br>AZT+3TC+DTG **or**<br>Any LPV/r or ATV/r regimen for < 2 years | **Switch all, regardless of VL**<br>Review VL in last 12 months:<br>**VL < 50:** continue normal VL monitoring<br>**VL ≥ 50:** switch, but do ABCDE assessment, provide EAC (if needed)<br>**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:<br>**TLD**<br>If client does not qualify for TDF:<br>**ABC + 3TC + DTG**<br>If client doesn't qualify for TDF and has ABC hypersensitivity:<br>**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**<br>If VL in last 12 months ≥ 50: switch, but do ABCDE assessment and provide EAC if needed.<br>Repeat VL after 3 months | No renal dysfunction, ≥ 10 years of age and weight ≥ 30 kg:<br>**TLD**<br>If client does not qualify for TDF:<br>**ABC + 3TC + DTG**<br>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 | | |

**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**

## 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
- Detection of current antiretroviral drugs in the client's blood or urine

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**

| 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 bd). 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 |

**[**]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**

## MONITORING WHILE ON ART

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

| MONTHS ON ART OR DC[Σ] | ROUTINE MONITORING TEST | OVERVIEW OF MANAGEMENT |
|---|---|---|
| 1 | Dispense two months ART<br>• FBC and diff (**if on AZT**) | **At every visit:**<br>• 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<br>• Counselling (travel plans, VL education)<br>• Integrated services for family planning and NCDs<br>• Do clinical assessment - weight; screen for TB and other OIs; WHO staging; pregnancy and discuss plans to conceive<br>• Ask about side effects |
| 3 | • VL<br>• sCr and eGFR (**if on TDF**)<br>• FBC and diff (**if on AZT**)<br>• Cholesterol and TG (**if on PI**). If high, do fasting cholesterol and TG. Obtain expert advice if still above acceptable range | |
| 4 | Review test results | • Renew prescription for 6 months, with first 3 month's supply issued today from the facility. Decant to preferred RPC if VL < 50, clinically well, no OIs (including TB) and not pregnant |
| 7 | Collect medication from preferred RPCs | |
| 10 | • VL<br>• sCr and eGFR (**if on TDF**)<br>• CD4 | • See "At every visit" above<br>• Check for TPT eligibility<br>• Renew prescription for 6 months<br>• Only recall patients with VL ≥ 50 or other abnormal result |
| 11+ | • Collect medication from preferred RPCs<br>• Annual clinical assessment (see "at every visit") and yearly GXP, regardless of symptoms<br>• **If on TDF:** repeat sCr and eGFR yearly<br>• **If on AZT:** repeat FBC and diff, if clinically indicated<br>• Do annual VLs from 10-12 DCs aligning with scripting cycle. Breastfeeding woman should have their VL monitored every 6 months from the time of delivery | |

**[Σ]DC = dispensing cycle, defined as the number of days for which a client would have treatment if a single standard "monthly" quantity of tablets was dispensed**

## CD4 MONITORING

| | |
|---|---|
| CD4 > 200 | Repeat CD4 at month/DC 10 on ART (align with VL) |
| CD4 ≤ 200 | Repeat at month/DC 10, 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

## VL MONITORING 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

| TLD < 2 years | TLD ≥ 2 years | |
|---|---|---|
| • Intensify efforts to resolve adherence issues<br>• Repeat VL at next scheduled routine VL | **Adherence < 80 % or persistent low-level viraemia (2 or more consecutive VLs** | **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** |
| | • Intensify adherence (ABCDE)<br>• Repeat VL at next scheduled routine VL | **TLD 1[#]**<br>**Clients who have never failed a previous ART regimen**<br>• Intensify adherence (ABCDE)<br>• Repeat VL at next scheduled routine VL<br>Do RT only:<br>• If client was incorrectly classified as TLD1; or<br>• Relevant drug interactions |
| | | **TLD 2**<br>**Clients who have failed a previous ART regimen**<br>• Discuss with an HIV expert to authorise and interpret RT<br>• 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***

**3TC**=lamivudine; **ABC**=abacavir; **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**=nucleoside 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; **TDF**=tenofovir; **tds**=three times daily; **TLD**=tenofovir + lamivudine + dolutegravir; **TLD 1**=clients on a DTG-containing regimen, who have never failed any other regimen (previous "first-line" terminology); **TLD 2**=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

Based on the 2023 ART Clinical Guidelines for the Management of HIV in Adults, Pregnancy, Adolescents, Children, Infants and Neonates, South African National Department of Health, April 2023

This publication was supported under funding provided by the Global Fund to Fight AIDS, Tuberculosis and Malaria through the National Department of Health of South Africa and the NDoH Pharmacovigilance Centre for Public Health Programmes. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Global Fund or the National Department of Health of South Africa