SOUTH AFRICAN ART CLINICAL GUIDELINES 2023

(Infants and children < 10 years and/or < 30kg)

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

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 (see below). Infants and children under five years, and those with advanced HIV disease should be prioritised for rapid initiation.
Same day initiation is encouraged if the child is clinically well

REASONS TO DEFER STARTING ART	WHEN TO INITIATE ART*
TB symptoms (cough, fever, night sweats, failure to thrive)	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: 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
Other acute illnesses e.g. *Pneumocystis jirovecii* pneumonia or bacterial pneumonia	Defer ART for 1 - 2 weeks after commencing treatment for the infection
Clinical symptoms or signs of liver disease	Do ALT and bilirubin. Investigate and manage possible causes

SOCIAL CONSIDERATIONS

The following points are important to maximise adherence:
- One named, responsible primary caregiver able to administer ART to the child
- Disclosure to another adult living in the same house able to supervise the child's ART when primary caregiver is unavailable

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

BASELINE CLINICAL EVALUATION

TEST AND PURPOSE	INTERPRETATION/ACTION
Recognise the client with respiratory, neurological or abdominal danger signs	Identify danger signs as classified in the IMCI Chart booklet. Refer urgently
Nutritional assessment To monitor growth, developmental stage and determine correct dosing of ART	Use the growth chart to plot the weight, height and head circumference (if < 2 years). Measure MUAC to identify moderate and severe malnutrition
Screen for symptoms of meningitis To diagnose and treat clients with cryptococcal and other forms of meningitis and reduce associated morbidity and mortality	Identify symptoms of headache, confusion or visual disturbances. Other symptoms may include fever, neck stiffness or coma. Do/refer the client for a lumbar puncture. Defer ART if meningitis is confirmed
Screen for TB To identify TB/HIV co-infection and eligibility for tuberculosis preventive therapy (TPT)	Suspect TB in clients with the following symptoms: coughing, night sweats, fever, failure to thrive. If present, confirm or exclude TB. Ask about TB contacts
WHO clinical staging To determine immune status, priority of initiating ART and need for cotrimoxazole preventive therapy (CPT)	See eligibility for CPT under CD4 cell count/% section in baseline laboratory evaluation below
Screen for active depression in older children and epilepsy in all ages To exclude drug-drug and drug-disease interactions	Identify the child with epilepsy and be aware of and monitor for potential drug-drug interactions and drug-disease interactions
Neurodevelopmental screen To identify neurocognitive or developmental delays	Screening tool is available in Road To Health Booklet (RTHB)

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. Infants < 1 month: HIV drug resistance test for infant if mother is failing treatment on TLD2 or a PI-based regimen
Haemoglobin (Hb) To identify anaemia and eligibility for AZT	Can use AZT if Hb ≥ 8 g/dL. Children with anaemia: < 5 years: Treat with iron supplementation and deworm child ≥ 5 years: Do FBC and manage according to Primary Health Care EML
CD4 cell count/% To determine eligibility for cotrimoxazole preventive therapy (CPT)	Eligibility for CPT: • All HIV-positive infants < 1 year irrespective of CD4 % or clinical stage • HIV-positive child 1 - 5 years with WHO stage 2, 3 or 4, or CD4 % ≤ 25 % • HIV-positive child under 5 years of age with PJP infection: start CPT after PJP treatment is completed • HIV-positive child > 5 years with WHO stage 2, 3 or 4, or CD4 ≤ 200
GeneXpert (MTB/Rif Ultra) To diagnose TB	Only for those with a positive TB symptom screen

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

ART REGIMENS IN NEW CLIENTS

≥ 3 kg to < 30 kg, **and** ≥ 4 weeks to < 10 years[##]	ABC + 3TC + DTG (dosing as per paed dosing chart)
Neonates[#] - birth to < 4 weeks of age (with birth weight ≥ 2.0 kg and ≥ 35 weeks gestational age at birth)	AZT + 3TC + NVP (see dosing below)

	Zidovudine (AZT)		Lamivudine (3TC)		Nevirapine (NVP)	
Available formulation	10 mg/mL		10 mg/mL		10 mg/mL	
Weight (kg) at birth	**Dose in mL**	**Dose in mg**	**Dose in mL**	**Dose in mg**	**Dose in mL**	**Dose in mg**
≥ 2 - < 3	1 mL BD	10 mg BD	0.5 mL BD	5 mg BD	1.5 mL BD	15 mg BD
≥ 3 - < 4	1.5 mL BD	15 mg BD	0.8 mL BD	8 mg BD	2 mL BD	20 mg BD
≥ 4 - < 5	2 mL BD	20 mg BD	1 mL BD	10 mg BD	3 mL BD	30 mg BD

Dosing is based on the birth weight of the child. It is not necessary to change the dose before 28 days of age if, for example, the weight decreases in the first week or two of life; Consult with a clinician experienced in paediatric ARV prescribing or the HIV hotline (0800 212 506), for neonates with birth weight < 2.0 kg or gestational age < 35 weeks, as well as infants ≥ 28 days of age but weight < 3 kg

[#]See protocol in the ART Clinical Guidelines for baseline testing and follow up for neonates < 4 weeks of age; [##] No VL needed when transitioning from NVP to DTG

SWITCHING EXISTING CLIENTS TO DTG-CONTAINING REGIMENS

NON VL-DEPENDENT REGIMEN SWITCHES

CURRENT REGIMEN	SWITCH TO:
Any LPV/r or ATV/r regimen for < 2 years	**ABC[*] + 3TC + DTG** If child is ≥ 30 kg and ≥ 10 years: switch client to TLD if eGFR > 80 mL/min. No additional VL needed before switch. Refer to Adult ART 2023 poster
ABC + 3TC + (EFV or NVP)	
AZT + 3TC + (EFV or NVP)	
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 but < 1000: switch, but do ABCDE assessment and provide EAC if needed	**ABC[*] + 3TC + DTG** Repeat VL after 3 months If child is ≥ 30 kg and ≥ 10 years: switch client to TLD if eGFR > 80 mL/min. Refer to Adult ART 2023 poster
Two or more consecutive VLs ≥ 1000 taken ≥ 2 years after starting LPV/r or ATV/r regimen	Adherence < 80 %	If already on LPV/r tablets: switch to DTG regimen	
		If on LPV/r solution or pellets: consider switch to 4-in-1 ABC/3TC/LPV/r capsules[$]. Repeat VL in 2-3 months	If repeat VL < 1000: **ABC[*] + 3TC + DTG** If child is ≥ 30 kg and ≥ 10 years: switch client to TLD if eGFR > 80 mL/min. Refer to Adult ART 2023 poster
			If repeat VL ≥ 1000: Discuss with HIV expert or the hotline (0800 212 506) to authorise and interpret a resistance test. Provide individualised regimen as recommended by HIV expert and repeat VL after 3 months to confirm re-suppression
	Adherence > 80 %	Discuss with HIV expert or the hotline (0800 212 506) to authorise and interpret a resistance test. Provide individualised regimen as recommended by HIV expert and repeat VL after 3 months to confirm re-suppression	
Only 1 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 in one of the above categories		

***If client has ABC hypersensitivity: AZT + 3TC + DTG; [$]If a switch to the 4-in-1 ABC/3TC/LPV/r capsules does not improve adherence, or is not available, continue to switch to ABC + 3TC + DTG as for non-adherent children on LPV/r tablets**

HOW TO MEASURE ADHERENCE OBJECTIVELY

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

CHILDREN CO-INFECTED WITH TUBERCULOSIS*

Children taking ART and TB treatment together will have to tolerate a large amount of medication. Intensify adherence support. Remember to add pyridoxine (vitamin B6) to TB treatment

DTG-based regimen	**AND** receiving a **rifampicin**-containing TB regimen: Boosting of DTG required while on rifampicin-containing TB treatment and until two weeks after rifampicin has been stopped. See ART Drug Dosing Chart for Children 2022
EFV-based regimen	No dose adjustments or changes in ART regimen needed for DS-TB treatment
LPV/r-based regimen	**AND** receiving a **rifampicin**-containing TB regimen: Additional **ritonavir** should be added or the LPV/r dose increased according to the ART Drug Dosing Chart for Children 2022. TB treatment should be dosed at standard doses. Stop additional ritonavir or increased LPV/r dose 2 weeks after TB-treatment completed

[*]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

VIRAL LOAD

WHEN: DC[€]/month 3, 10 and every 12 DCs
For < 5 year olds done at week 14 (DC 4), month 12 (DC 13) and then at 12 DC intervals

Remember a VL ≥ 50 is a medical emergency!

RESPONSE TO VL ON DTG REGIMEN

- **VL < 50:** Continue yearly monitoring
- **VL ≥ 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. Repeat VL after 3 months. Also see section on CD4 monitoring

RESPONSE TO REPEAT VL ON DTG REGIMEN

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

CLINICAL ASSESSMENT

WHEN: every visit

- Height, weight, head circumference (< 2 years) and neurodevelopment (remember to adjust ART dosage according to weight)
- Ask about side-effects
- TB & other opportunistic infection screen
- WHO staging

CD4 COUNT

WHEN: after 10 DCs[€] on ART (aligned with VL)
- **Repeat 6 monthly:** if CD4 ≤ 200 **OR** VL ≥ 1000 cells/µL
- **Repeat if:** any clinical indication arises (i.e. new WHO stage 3 or 4) **OR** a client missed a scheduled visit by > 90 days

INTERPRETATION: Stop cotrimoxazole once ART-associated immune reconstitution has occurred:
- **HIV-positive infants < 12 months**: should remain on CPT
- **HIV-positive child 1 – 5 years:** If CD4 percentage ≥ 25% (If previous PJP, stop at 5 years old if meets ≥ 5 years category)
- **HIV-positive child ≥ 5 years:** If CD4 count ≥ 200 cells/µL

RESPONSE TO REPEAT VL ON DTG REGIMEN, IF VL > 50

DTG regimen < 2 years

- Intensify efforts to resolve adherence issues
- Repeat VL at next scheduled routine VL

DTG regimen ≥ 2 years

Adherence > 80 %, **AND** with 2 or more VLs ≥ 1000 taken ≥ 2 years after starting DTG regimen **OR** at least one VL ≥ 1000 and either CD4 < 200 or an opportunistic infection

Clients who have failed a previous ART regimen:
Discuss with an HIV expert to authorise and interpret RT.
Do VL 3 months after new regimen implemented

Clients who have never failed a previous ART regimen:
Intensify adherence (ABCDE)
- Repeat VL at next scheduled routine VL

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

Do RT only:
- if client was incorrectly classified as a client who has never failed a ART regimen; or
- Relevant drug interactions

Adherence still suboptimal (adherence < 80 %) or persistent low-level viraemia (2 or more consecutive VLs between 50 and 999)
- Intensify adherence (ABCDE)
- Repeat VL at next scheduled routine

[€]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

DO THE FOLLOWING TESTS IF THE CLIENT IS ON THE DRUG THAT MAY CAUSE THE ADVERSE EVENT

DRUG	TEST	FREQUENCY	ACTION/INTERPRETATION
AZT	FBC + differential WCC	At months 1 and 3, thereafter if clinically indicated	Hb ≥ 8 g/dL: Continue AZT Hb < 8 g/dL or neutrophil count persistently < 1000 cells/µL: Use alternative – consult with expert
PI-based regimen (LPV/r, ATV/r, DRV/r)	Cholesterol + Triglycerides (TG)	At month 3, if above acceptable range, do fasting cholesterol and TG	To monitor PI-related metabolic side-effects. If fasting cholesterol and TG are still above the acceptable range, obtain expert advice
TB treatment **or** NVP **or** EFV	ALT	If signs/symptoms of hepatitis (e.g. nausea, vomiting, jaundice)	If ALT is abnormal, refer to specialist or phone the HIV hotline (0800 212 506)
NVP	ALT	If rash develops	If ALT is abnormal, refer to specialist or phone the HIV hotline (0800 212 506)

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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; **EML** = essential medicines list; **FBC** = full blood count; **FTC** = emtricitabine; **HBV** = hepatitis B virus; **HBsAg** = hepatitis B surface antigen; **IMCI** = Integrated management of childhood illness; **InSTI** = Integrase strand transfer inhibitor; **LPV/r** = lopinavir and ritonavir; **LP** = lumbar puncture; **MUAC** = mid-upper arm circumference; **NCD** = non-communicable disease; **NRTI** = nucleoside reverse transcriptase inhibitor; **NNRTI** = non-nucleoside reverse transcriptase inhibitor; **NVP** = nevirapine; **Paed** = paediatric; **PI** = protease inhibitor; **OI** = opportunistic infection; **PJP** = *Pneumocystis jirovecii* pneumonia; **RPC** = repeat prescription collection; **RT** = resistance test; **TB** = Tuberculosis; **TBM** = Tuberculosis meningitis; **TC** = total cholesterol; **TDF** = tenofovir; **TLD** = tenofovir + lamivudine + dolutegravir; **TEE** = tenofovir + emtricitabine + efavirenz; **TG** = Triglycerides; **TPT** = TB preventive therapy; **VL** = viral load; **WCC** = white cell count