SOUTH AFRICAN ART CLINICAL GUIDELINES 2019

(Infants and children < 10 years or < 35kg)

First edition February 2020

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 client is clinically well and motivated

REASONS TO DEFER STARTING ART	WHEN TO START ART*
TB symptoms (cough, fever, recent weight loss, fatigue/always tired)	No TB: Same day or within 7 days <u>Confirmed DS-TB at non-neurological site:</u> CD4 < 50 cells/µL: within 2 weeks of starting TB treatment CD4 ≥ 50 cells/µL: within 8 weeks after starting TB treatment <u>Confirmed DR-TB at non-neurological site:</u> 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
Serum CrAg-positive with no symptoms or signs of meningitis	2 weeks after starting fluconazole
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 before starting ART

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 if needed
Height, weight, head circumference (< 2 years), and measure MUAC Nutritional assessment to monitor growth, developmental stage and determine correct dosing of ART	Use the Road to Health Booklet (RTHB) as tool
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. 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, unexplained weight loss, then confirm or exclude TB. Do GeneXpert in clients with a positive TB symptom screen
WHO clinical staging To determine immune status, priority of initiating ART and need for cotrimoxazole preventive therapy (CPT)	See eligibility for CPT under CD4 count section in baseline laboratory evaluation, below
Screen for depression in older children and epilepsy in all ages To exclude drug-drug and drug-disease interactions	Be aware of and monitor for potential drug interactions and neuropsychiatric side effects of efavirenz and dolutegravir
Neurodevelopmental screen To identify neurocognitive or developmental delays	Refer the child to the next level of care if child has not achieved the age-appropriate developmental milestone. Screening tool is available in RTHB

BASELINE LABORATORY EVALUATION (> 1 MONTH OLD)

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
Haemoglobin (Hb) To identify anaemia and eligibility for AZT	Can use AZT if Hb ≥ 8 g/dL Treat anaemia according to Primary Health Care EML
CD4 cell count To determine eligibility for cotrimoxazole preventive therapy (CPT)	<u>Eligibility for CPT:</u> · All HIV-positive children ≥ 4 weeks and < 1 year · HIV-positive child 1 - 5 years with WHO stage 2, 3 or 4, or CD4 ≤ 25% · HIV-positive child > 5 years with WHO stage 2, 3 or 4, or CD4 ≤ 200

REGIMENS

FIRST-LINE ART IN NEW CLIENTS

Neonates[#] until 28 days of age (with birth weight ≥ 2.5 kg)	AZT + 3TC + NVP (see dosing below)

	Lamivudine (3TC)		Zidovudine (AZT)		Nevirapine (NVP)	
Target dose	2 mg/kg/dose TWICE daily (BD)		4 mg/kg/dose TWICE daily (BD)		6 mg/kg/dose TWICE daily (BD)	
Available formulation	10 mg/mL		10 mg/mL		10 mg/mL	
Weight (kg)	**Dose in ml**	**Dose in mg**	**Dose in ml**	**Dose in mg**	**Dose in ml**	**Dose in mg**
≥ 2.5 - < 3	0.5 mL BD	5 mg BD	1 mL BD	10 mg BD	1.5 mL BD	15 mg BD
≥ 3 - < 4	0.8 mL BD	8 mg BD	1.5 mL BD	15 mg BD	2 mL BD	20 mg BD
≥ 4 - < 5	1 mL BD	10 mg BD	2 mL BD	20 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
- Caregivers administering ARV medication to the child must be supplied with a syringe (2 mL or 5 mL) for each of the 3 ARVs and shown how to prepare and administer the prescribed dose. If required, bottles and syringes should be colour coded with stickers and a sticker of the relevant colour used to mark the correct dose on the syringe.

[#] See protocol in the 2019 ART Clinical Guidelines for baseline testing and follow up for neonates < 4 weeks of age; Consult with a clinician experienced in paediatric ARV prescribing or the HIV hotline (0800 212 506), for neonates with birth weight < 2.5 kg or gestational age < 35 weeks, as well as infants ≥ 28 days of age but < 42 weeks corrected gestational age or weight < 3 kg

≥ 4 weeks of age, **<u>and</u>** ≥ 42 weeks gestational age **<u>and</u>** ≥ 3 kg, but < 20 kg	ABC + 3TC + LPV/r
≥ 20 kg to < 35 kg or < 10 years of age	ABC + 3TC + DTG
≥ 35 kg and ≥ 10 years of age	Transition to adult and adolescent regimens

SWITCHING TO DTG IN CHILDREN WHO ARE ON FIRST-LINE PAEDIATRIC REGIMENS

Before switching to DTG, discuss risks and benefits with caregiver and only switch if caregiver chooses to switch

To switch, client must:
- Weigh ≥ 20 kg[Ψ], **and**
- VL < 50 (in the last 6 months) **or**
- VL 50 – 999 in the last 6 months and on repeat VL after 3 months VL is ≤ 999 copies/mL

Current regimen	New regimen
ABC + 3TC + LPV/r	ABC + 3TC + DTG
ABC + 3TC + EFV	

Ψ If child is ≥ 35 kg and ≥ 10 years: refer to adolescent and adult poster for changing ABC to TDF

SECOND- AND THIRD-LINE REGIMENS WITH CONFIRMED VIROLOGICAL FAILURE

All children with confirmed virological failure should be discussed with an expert

	NNRTI-BASED REGIMEN		PI-BASED REGIMEN FOR > 2 YEARS[¥]			INSTI-BASED REGIMEN FOR > 2 YEARS[¥]	
Regimen	(ABC or AZT) + 3TC + **(EFV or NVP)**		(ABC or AZT) + 3TC + **(LPV/r or ATV/r)**			(ABC or AZT) + 3TC + **DTG**	
Resistance Testing	Resistance test **<u>not</u>** required		Resistance test required. PI resistance present or genotype unsuccessful?			Resistance test required. InSTI resistance present?	
			No		Yes	No	Yes
Weight	< 20 kg	≥ 20 kg	< 20 kg	≥ 20 kg	All	All children on DTG will be ≥ 20 kg	
New regimen	(AZT or ABC) + 3TC + LPV/r	**2 NRTIs + DTG** In consultation with an expert ensure at least one active NRTI[#] If NRTI activity cannot be confirmed: **2 NRTIs + PI/r**	Continue current regimen and address adherence	**2 NRTIs + DTG** In consultation with an expert ensure at least one active NRTI[#] If NRTI activity cannot be confirmed: **2 NRTIs + PI/r**	Refer to third-line committee	**2 NRTIs + DTG** In consultation with an expert ensure at least one active NRTI[#] If NRTI activity cannot be confirmed: refer to third-line committee	Refer to third-line committee

[¥] In some cases, for example where LPV/r wasn't dose adjusted with rifampicin containing TB-treatment, a resistance test may be considered sooner. Discuss with an expert;
[#] AZT can be used if the client has only been exposed to ABC previously. Discuss with expert if unsure

Based on the 2019 ART Clinical Guidelines for the Management of HIV in Adults, Pregnancy, Adolescents, Children, Infants and Neonates

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FOLLOW-UP TESTING IN CLIENTS ON ART

At **every** visit:
- Height, weight, head circumference (< 2 years) and development (remember to adjust ART dosage according to weight)
- Clinical assessment
- Ask about side-effects
- TB & other opportunistic infection screen
- Neurocognitive assessment
- WHO staging

TEST	ACTION/INTERPRETATION
CD4 count (cells/µL) At month 12 on ART. Repeat 6 monthly if VL ≥ 1000 or until client meets criteria to stop CPT	Stop cotrimoxazole once ART-associated immune reconstitution has occurred: • **HIV-positive infants < 12 months** should remain on CPT • **1 – 5 years:** If CD4 percentage ≥ 25% (If previous PJP, stop at 5 years old if meets ≥ 5 years category) • **≥ 5 years:** If CD4 count ≥ 200
Viral Load (VL) (copies/mL) Month 6, 12 and then 12-monthly if VL suppressed	

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. Repeat VL in 3 months <u>If VL still ≥ 1000 and child on **NNRTI-based** regimen:</u> Consider switching to second-line if virological failure confirmed, i.e. VL ≥ 1000 on 2 consecutive occasions and adherence issues addressed <u>If VL still ≥ 1000 and child is on **PI- or InSTI (DTG)-based** regimen:</u> Do resistance testing 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)
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 in 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. Client is doing well

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 3 and 6, 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 TG > 10, refer. If TC elevated, 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)

CHILDREN WITH CONCOMITANT 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. The dosing frequency of DTG should be increased to 50 mg 12 hourly while on rifampicin-containing TB treatment and until two weeks after rifampicin has been stopped
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 paediatric dosing chart. TB treatment should be dosed at standard doses. Stop additional ritonavir or increased dose 2 weeks after TB-treatment completed

3TC = lamivudine; **ABC** = abacavir; **ART** = antiretroviral therapy; **ATV/r** = atazanavir and ritonavir; **AZT** = zidovudine; **CM** = cryptococcal meningitis; **CPT** = cotrimoxazole preventive therapy; **CrAg** = cryptococcal antigen; **DTG** = dolutegravir; **DRV/r** = darunavir and ritonavir; **DS** = drug-sensitive; **DR:** drug-resistant; **EFV** = efavirenz; **eGFR** = estimated glomerular filtration rate; **HBV** = hepatitis B virus; **HBsAg** = hepatitis B surface antigen; **InSTI** = integrase strand transfer inhibitor; **LPR/r** = lopinavir and ritonavir; **LP** = lumbar puncture; **MUAC** = Middle upper arm circumference; **NRTI** = nucleoside reverse transcriptase inhibitor; **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; **WCC** = white cell count; **VL** = viral load