# WESTERN CAPE ART GUIDELINES 2019

## (INFANTS AND CHILDREN < 10 YEARS OR < 35 KG)

October 2020, 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

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. Eligible children should have developmental and clinical assessments, TB screening and HIV clinical staging done before initiating ART. Caregivers must receive counselling on how to administer medication, monitor side-effects and deal with challenges to adherence. Eligible children should be started on ART as soon as possible. Fast-track children (start ART within 7 days) in the following situations: infants, children < 5 years of age, WHO clinical stage 4, CD4 ≤ 200 or < 15%

| 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<br>Confirmed DS-TB at non-neurological site:<br>CD4 < 50 cells/µL or < 15%: within 2 weeks of starting TB treatment<br>CD4 ≥ 50 cells/µL or ≥ 15%: 2 - 8 weeks of starting TB treatment<br>Confirmed DR-TB at non-neurological site:<br>Start ART 2 weeks after TB treatment, once symptoms improved and TB treatment tolerated |
| Signs and symptoms of meningitis (headache, fever, confusion, 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 |
| 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 |

*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 present |
| **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 patients 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 |
| **Genotype resistance test in newly diagnosed infants < 2 years of age if mother was exposed to PI-based ART during pregnancy and breastfeeding -** To screen for baseline resistance to PIs | Discuss with expert if PI resistance present |
| **FBC + differential WCC -** To identify anaemia, neutropenia, thrombocytopenia and eligibility for AZT | Can use AZT if Hb ≥ 8 g/dL<br>Treat anaemia according to Primary Health Care EML |
| **CD4 cell count -** To determine need for cotrimoxazole preventive therapy (CPT) | Eligibility for CPT:<br>· All HIV-positive children ≥ 4 weeks and < 1 year<br>· HIV-positive child 1-5 years with WHO stage 2, 3 or 4, or CD4 ≤ 25%<br>· HIV-positive child > 5 years with WHO stage 2, 3 or 4, or CD4 ≤ 200 |
| **ALT -** If jaundiced or on TB treatment | Baseline test |

## REGIMENS

### RECOMMENDED FIRST-LINE ART IN NEW PATIENTS

| | |
|---|---|
| **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 | 10mg/mL | | 10mg/mL | | 10mg/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 with weight < 3kg

| | |
|---|---|
| ≥ 4 weeks of age, **and** ≥ 42 weeks gestational age **and** ≥ 3 kg, but < 20kg | 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 |

** ATV/r can be used instead of LPV/r due to hyperlipidaemia, severe gastrointestinal side effects > 6 weeks on LPV/r or to simplify regimen to once daily

### 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, patient must:
Weigh ≥ 20 kg$^{\Psi}$, **and** VL < 50 (in the last 6 months)

| Current regimen | New regimen |
|---|---|
| ABC + 3TC + (LPV/r or ATV/r) | ABC + 3TC + DTG |
| ABC + 3TC + EFV | |

$^{\Psi}$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 **not** required | | Resistance test required. PI resistance present or genotype unsuccessful? | | | Resistance test required. InSTI resistance present? | |
| | | | No$^{\Phi}$ | | 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$^{\varpi}$<br>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$^{\varpi}$<br>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$^{\varpi}$<br>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; $^{\varpi}$AZT can be used if the patient has only been exposed to ABC previously. Discuss with an expert if unsure; $^{\Phi}$Patients who are failing PI-based regimens with no PI-mutations on genotype are most probably non-adherent to ART

Based on the Western Cape Consolidated Guidelines for HIV Treatment: Prevention of Mother-to-Child Transmission of HIV (PMTCT), Children, Adolescents and Adults 2019., amended July 2020.

## FOLLOW-UP MONITORING IN PATIENTS 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 until client meets criteria to stop CPT or repeat 6 monthly if two consecutive VLs ≥ 50 | Stop cotrimoxazole once ART-associated immune reconstitution has occurred:<br>• **HIV-positive infants < 12 months** should remain on CPT<br>• **1 – 5 years:** If CD4 percentage ≥ 25% (If previous PJP stop at 5 years old if meets > 5 years category)<br>• **> 5 years:** If CD4 count ≥ 200 |
| **Viral Load (VL) (copies/mL)**<br>Children on first-line: Month 4, 12 and then 12-monthly if virologically suppressed<br>Children on second- or third-line: Month 6, 12 and then 12-monthly if virologically suppressed<br>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. Repeat VL in 3 months<br>If VL still ≥ 1000 and child 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<br>If VL still ≥ 1000 and child is on **PI- or InSTI (DTG)-based** regimen:<br>Do resistance testing:<br>• if virological failure confirmed, i.e. VL ≥ 1000 on at least 3 occasions over the course of 2 years,<br>• or VL ≥ 1000 with signs of immunological or clinical failure (i.e. declining CD4 and/or opportunistic infections, intolerance, not taking medicines well). Discuss with expert<br>• or VL ≥ 1000 for < 2 years with no dose adjustments of PI or DTG with 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 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. Patient is doing well |

## LABORATORY MONITORING WHILE ON ART

| DRUG | TEST | FREQUENCY | ACTION/INTERPRETATION |
|---|---|---|---|
| AZT | FBC + differential WCC | At months 1, 3 and 6, thereafter if clinically indicated | Hb ≥ 8 g/dL: Continue AZT<br>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 | At month 3, if above acceptable range discuss with expert | To monitor PI-related metabolic side-effects. If TG > 10, refer. If TC elevated, obtain expert advice. Consider switch to ATV/r if > 6 years old and ≥ 15kg |
| 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 immediately or phone the HIV hotline |

## TB/HIV CO-INFECTION

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. Contraindicated with bedaquiline |
| **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 |
| **ATV/r**-based regimen | **ATV/r** is contraindicated with rifampicin. Change rifampicin to rifabutin. Discuss dose with expert |

**3TC** = lamivudine; **ABC** = abacavir; **ART** = antiretroviral therapy; **ATV/r** = atazanavir and ritonavir; **AZT** = zidovudine; **CM** = cryptococcal meningitis; **CPT** = co-trimoxazole 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; **FBC** = full blood count; **HBV** = hepatitis B virus; **HBsAg** = hepatitis B surface antigen; **InSTI** = integrase strand transfer inhibitor; **LPV/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; **PJP** = *Pneumocystis jirovecii* pneumonia; **TB** = tuberculosis; **TBM** = tuberculosis meningitis; **TLD** = tenofovir + lamivudine + dolutegravir; **TEE** = tenofovir + emtricitabine + efavirenz; **TC** = total cholesterol; **TG** = triglycerides; **VL** = viral load