SOUTH AFRICAN ANTIRETROVIRAL TREATMENT GUIDELINES 2015

(Infants > 4 weeks, children & early adolescents < 15 years)

THIRD EDITION FEBRUARY 2018

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

ELIGIBILITY CRITERIA

All HIV positive children, irrespective of CD4 or clinical staging

WHEN TO START

PATIENTS REQUIRING FAST TRACK

START ANTIRETROVIRAL TREATMENT (ART) WITHIN 7 DAYS OF BEING ELIGIBLE

- Children < 1 year
- WHO clinical stage 4
- MDR- or XDR-TB
- CD4 ≤ 200 cells/μL or ≤ 15 %

SOCIAL CONSIDERATIONS

The following points are important to maximise adherence:

- One identifiable caregiver who is able to supervise the child for administering medication
- Disclosure to another adult living in the same house, to supervise the child's ART when the other caregiver is unavailable
- Treatment of mother/caregiver/other family member is to be encouraged

REGIMENS

1ST LINE

Neonates (infants ≤ 4 weeks old)	Refer to guideline on initiation of ART in infants ≤ 4 weeks, or phone the HIV hotline (0800 212 506)	
≥ 4 weeks < 3 years (or < 10kg)	ABC + 3TC + LPV/r	**When children turn 3 years old, they are NOT routinely changed from LPV/r to EFV. Refer to HIV Hotline for patient-specific cases**
≥ 3 years and ≥ 10kg	ABC + 3TC + EFV (Use NVP if EFV contra-indicated)	
Adolescents ≥ 15 years **AND** ≥ 40 kg **AND** CrCl > 80 mL/min	TDF + FTC (or 3TC) + EFV Provided as fixed dose combination (FDC)	Follow adult guidelines
Currently on **d4T**-based regimen	Change d4T to **ABC** if viral load (VL) is **undetectable** (< 40 copies/mL) If VL > 1000 copies/mL: Manage as possible treatment failure If VL 40 – 1000 copies/mL: Consult with expert or phone the HIV hotline	
Currently on **ddI** containing regimen	Change ddI to **ABC**, regardless of VL	

TRANSITION FROM ADOLESCENT TO ADULT GUIDELINE

Adolescents currently on (**ABC or d4T**) + 3TC + EFV:

Switch to FDC (TDF + FTC + EFV) if > 15 years **AND** > 40 kg **AND** CrCl > 80 mL/min, no proteinuria and virally suppressed (VL done within the last 8 weeks). If proteinuria > 1+ and CrCl < 80, refer to an expert

Adolescent < 16 years:

$$\text{CrCl (mL/min)} = \frac{\text{height (cm)}}{\text{serum creatinine (μmol/L)}} \; x\, 40$$

2ND LINE

Failed 1st line Protease Inhibitor (PI)-based regimen

Failed regimen	Action
ABC + 3TC + **LPV/r**	**Manage as for 3rd line – see below**
d4T + 3TC + **LPV/r**	
Unboosted PI-based regimen, while taking rifampicin	

Failed 1st line NNRTI-based regimen

Failed regimen	Action
ABC + 3TC + **EFV (or NVP)**	**AZT** + 3TC + **LPV/r**
d4T + 3TC + **EFV (or NVP)**	**AZT + ABC + LPV/r**

3RD LINE

Failing 2nd line regimen	Managed by a Paediatric Infectious Diseases specialist on the basis of genotype resistance testing. Phone the HIV hotline for further assistance (0800 212 506)

MONITORING

BASELINE

Test	Purpose	Interpretation/Action
Height, weight, head circumference (< 2 years) and development	To monitor growth, developmental stage and determine correct dosing of ART	Use the "Road to Health" chart as tool
Verify HIV status	Ensure that the national testing algorithm has been followed	Follow testing algorithm as per guidelines and document HIV status clearly
Screen for TB symptoms	To identify TB/HIV co-infection	Suspect TB in patients with the following symptoms: coughing, night sweats, unexplained weight loss, then confirm or exclude TB
WHO Clinical staging (≥ 5 years) and CD4 count (if not performed in last 6 months)	To determine immune status of patient, priority for initiating ART and the need for co-trimoxazole prophylaxis (CPT)	CD4 ≤ 350 cells/μL: Immediate priority CD4 ≤ 200 cells/μL: Fast track patient Eligibility for co-trimoxazole prophylaxis (CPT): • HIV-positive children > 4 weeks and < 1 year, regardless of CD4 • HIV-positive child 1-5 years with WHO stage 2,3 or 4; CD4 < 25% or < 500 • HIV-positive child > 6 years with WHO stage 3 or 4, CD4 < 350
FBC + differential WCC	To detect anaemia, neutropaenia or thrombocytopaenia	If Hb < 8 g/dL, start ART and refer patient for management of anaemia (AZT not recommended if Hb < 8)
Neurocognitive development assessments	To identify neurocognitive or developmental delays	Refer the child to the next level of care if child has not achieved the developmental milestone

INCLUDE THE FOLLOWING BASELINE TESTS IF PATIENT IS STARTING ART WITH

	Test	Purpose
LPV/r	Cholesterol and triglycerides	Baseline assessment
TB treatment or jaundiced	ALT	To assess for liver dysfunction

FOLLOW-UP TESTING IN PATIENTS ON ART

At **every** visit:

- Height, weight, head circumference (< 2 years) and development
- Clinical assessment
- Ask about side-effects
- TB Screen
- Neurocognitive assessment

Test and frequency	Action/Interpretation
CD4 count (cells/μL) At 1 year on ART, and annually if clinically indicated	Stop co-trimoxazole once ART-associated immune reconstitution has occurred for ≥ 6 months, i.e. CD4 count is as follows on TWO consecutive occasions 3 to 6 months apart: **1 – 5 years:** CD4 ≥ 500 cells/μL (If previous PCP stop at 5 years old) **≥ 6 years:** CD4 ≥ 350 cells/μL HIV-positive infants < 12 months should remain on CPT
VL (copies/mL) Month 6, 12 and then annually	**VL copies/mL** / **Response** > 1000: Begin step-up adherence; Repeat VL after 2-3 months; If VL still > 1000 despite good adherence and child on **NNRTI** regimen: discuss with expert about switching to second line; If VL still > 1000 despite good adherence and child is on **PI-based** regimen: reinforce adherence, see section on 3rd line 50 – 1000: Begin step-up adherence; Repeat VL in 6 months < 50: Repeat VL annually; and routine adherence support. Patient is doing well

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

Drug	Test	Frequency	Action/Interpretation
AZT	Hb or FBC	Month 1,2,3 and then annually	Hb > 8 g/dL: Continue AZT Hb ≤ 8 g/dL: Use alternative – consult with expert
LPV/r	Cholesterol + triglycerides (preferably fasting)	Annually	To monitor PI-related metabolic side-effects. Consult with specialist if a significant difference is noted from patient's previous lipid profile and advise dietary modification
TB treatment, **or** NVP, **or** EFV	ALT	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)

Based on the National Consolidated Guidelines for the Prevention of Mother-to-Child Transmission of HIV (PMTCT) and the Management of HIV in Children, Adolescents and Adults. National Department of Health, South Africa. April 2015. Updated November 2016 to incorporate the National Test and Treat protocol implemented by NDoH, Sep 2016.

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Third edition: February 2018

CHILDREN WITH CONCOMITANT TUBERCULOSIS

Children taking ART and TB treatment together will have to tolerate a large number of pills. Intensify adherence support. Always review viral suppression if on ART for more than 6 months

CURRENT ART REGIMEN	RECOMMENDATIONS
EFV-based regimen	No dose adjustments or changes in ART regimen and standard dose TB treatment should be added
LPV/r-based regimen	**AND** receiving a **rifampicin**-containing TB regimen: Additional **ritonavir** should be added according to the paediatric dosing chart. TB treatment should be dosed at standard doses. Stop ritonavir 2 weeks after TB-treatment completed

ISONIAZID PREVENTIVE THERAPY

INDICATIONS

- HIV-positive children irrespective of age, with a direct pulmonary TB contact (someone with TB who resides with the child), after active TB has been excluded in the child by X-ray and symptom screening (symptoms include: coughing, night sweats, unexplained weight loss, persistent fever of more than two weeks, poor weight gain, fatigue)
- HIV infected children 5 – 14 years without history of close contact but tuberculin skin test (TST) positive

Consult with specialist if close contact has confirmed or suspected drug resistant TB

DOSAGE AND ADMINISTRATION

Isoniazid (INH) 10 mg/kg/day for 6 months (max dose: 300 mg daily)

Crush appropriate fraction of the 100 mg INH tablet and dissolve in water or multivitamin syrup before giving it to the child

Add pyridoxine (Vitamin B6) 25 mg daily in children > 5 years, or 12.5 mg daily in children < 5 years for duration of IPT

PRACTICAL ADVICE FOR ADMINISTRATION OF ARVs

- It is important to check regularly that children receive the correct dose, based on their weight
- In older children or adolescents ensure that maximum doses are not exceeded
- Always prescribe fixed dose combinations if appropriate

ARV	ADVICE
Abacavir (ABC)	Advise caregivers about the potential hypersentivity reaction which usually occurs within the first 6 weeks of treatment. If patient on ABC develops fever, rash, gastrointestinal or respiratory symptoms, the patient should be taken to the hospital. In patients who have had a hypersensitivity reaction, ABC would be stopped and never rechallenged. All tablet formulations, except the 60 mg tablet, must be swallowed whole and NOT chewed, divided or crushed
Efavirenz (EFV)	Tablets must not be chewed, divided or crushed; swallow whole with or without food e.g. yoghurt or banana. Capsules may be opened and powder contents dispersed in water or mixed with a small amount of food (e.g. yoghurt) to disguise peppery taste. Ingest immediately. Food, especially high-fat meals, increases absorption. Best given at bedtime to reduce CNS side effects, especially during first 2 weeks
Lamivudine (3TC)	No food restrictions, oral solution may be stored at room temperature. Tablets are scored and can be easily divided; may be crushed and mixed with a small amount of water or food and ingested immediately
Lopinavir/ ritonavir (LPV/r) Aluvia® OR Kaletra®	Dose is calculated on lopinavir component. Solution is best taken with food as it increases absorption. If there is no food, then the patient can take the medicine without food. Solution should be refrigerated. If no fridge is available, it can be stored at room temperature of 25˚C for 6 weeks. Techniques to increase tolerance & palatability: coat mouth with peanut butter, dull taste buds with ice, follow dose with sweet foods. Tablets must not be chewed, divided or crushed; swallow whole with or without food. Many drug interactions
Nevirapine (NVP)	Once-daily dosing during the first 2 weeks of treatment reduces frequency of rash. If a mild rash occurs during the induction period, continue once daily dosing and only escalate dose to twice daily once the rash has subsided and the dose is well tolerated. NVP should be permanently discontinued and not restarted in children who develop severe rash, especially if accompanied by fever, blistering or mucosal ulceration. No food restrictions. Tablets can be crushed and mixed with a small amount of water or food and immediately ingested. Consider drug-drug interactions
Ritonavir (RTV)	Only recommended use at present is as a booster for lopinavir/ritonavir when coadministered with rifampicin-containing TB treatment. Should be taken with food. May be stored at room temperature, limited shelf life of 6 months. May need to use techniques described for Kaletra® to improve tolerance of bitter taste
Stavudine (d4T)	Capsules may be opened and powder contents dispersed in water (stable in solution for 24 hours) or mixed with a small amount of food (e.g. yoghurt)
Zidovudine (AZT)	No food restrictions and oral solution may be stored at room temperature. Capsules may be opened and powder contents dispersed in water or mixed with a small amount of food (e.g. yoghurt) and immediately ingested. Currently available tablets are not scored. Use with caution in children with anaemia, due to potential for bone marrow suppression