SOUTH AFRICAN ANTIRETROVIRAL TREATMENT GUIDELINES (ADULT) 2016

NEED HELP?

Contact the TOLL-FREE National HIV & TB Health Care Worker Hotline

0800 212 506 /021 - 406 6782

Alternatively send an SMS or "Please Call Me" to 071 840 1572

www.mic.uct.ac.za

When to start ART in HIV-positive patients

Eligible to start ART

All HIV positive patients, irrespective of CD4 count or clinical staging

Timing of ART Initiation

Fast track initiation
- Patients with CD4 ≤ 200 cells/μL
- WHO HIV Stage 4, irrespective of CD4 count

Immediate priority
- Pregnant or breastfeeding patients, with no active TB or contraindication to first line ART
- All HIV positive adolescents and adults with CD4 ≤ 350 cells/μL

Delay initiation of ART in the following patients

- Cryptococcal meningitis (CM) or TB meningitis (TBM): delay ART initiation for 4 – 6 weeks
- Tuberculosis (TB):
  - If CD4 < 50 cells/mm3, start ART within 2 weeks after starting TB treatment
  - If CD4 > 50 cells/mm3, start ART within 8 weeks after starting TB treatment

This is to allow for improvement of patient's symptoms and ensure TB treatment is tolerated

Regimens

1st line

All **NEW PATIENTS** eligible for ART, including: • pregnant and breastfeeding women • HBV or TB co-infection • adolescents ≥ 15 years AND ≥ 40 kg AND CrCl* > 80 mL/min	**TDF + FTC (or 3TC) + EFV** Provided as fixed dose combination (FDC)
Adults on **d4T**-based regimen: Change d4T to TDF if virally suppressed and eGFR**/CrCl > 50mL/min. If viral load (VL) > 1000, do NOT change and manage as potential treatment failure	**TDF** + FTC (or 3TC) + EFV FDC preferred
Adolescents# on (ABC or d4T) + 3TC + EFV: switch to FDC if ≥ 15 years, weigh ≥ 40 kg, CrCl > 80 mL/min, no proteinuria and virally suppressed (VL done within the last 8 weeks)	
Adolescent < 40 kg and < 15 years	ABC + 3TC + EFV (Dose according to paediatric dosing chart)

Alternative 1st line regimens

Contraindications to **EFV**: • Significant psychiatric co-morbidities **OR** • Intolerance to EFV **OR** • EFV may impair daily functioning e.g. shift workers	TDF + FTC (or 3TC) + **NVP**
Contraindication to **EFV** (see above) and to **NVP** (see below): • Baseline CD4 ≥ 250 for females • Baseline CD4 ≥ 400 in male patients	TDF + FTC (or 3TC) + **LPV/r**
Contraindication to **TDF**: • Renal disease (eGFR/CrCl < 50 mL/min) • The use of other nephrotoxic drugs e.g. aminoglycosides (kanamycin, amikacin)	**ABC** + 3TC + EFV (or NVP)

2nd line

Failing on a **TDF**-based 1st line regimen	Hepatitis B surface antigen (HBsAg) **negative**	AZT + 3TC + LPV/r
	HBsAg **positive**	TDF + AZT + 3TC + LPV/r
Failing on a **d4T**- or **AZT**-based 1st line regimen		TDF + 3TC (or FTC) + LPV/r

Alternative 2nd line regimens

Patients with anaemia and renal failure	**ABC** + 3TC + LPV/r
Dyslipidaemia (Total Cholesterol > 6 mmol/L) or intractable diarrhoea associated with **LPV/r**	Switch LPV/r to ATV/r

3rd Line

Failing any 2nd line regimen	Specialist referral – Regimen should be chosen according to genotype resistance testing, managed by an expert panel. Third line drugs will be managed centrally

Eligibility for genotype resistance testing

Taking a PI-based regimen for > 1 year, **AND** VL > 1000	• Address adherence, tolerability, regimen drug-drug interactions & assess psychological issues • Repeat VL after 6 months • After 6 months if VL still > 1000: consider genotyping

*CrCl = creatinine clearance **eGFR = estimated glomerular filtration rate

#Please note that the Cockroft-Gault formula does NOT apply to children or adolescents. Using it in these groups will result in an incorrect CrCl. Please call the hotline for further information

Monitoring pre-ART

- Verify HIV status
- CD4 count
- WHO staging
- Screen for TB, STIs and pregnancy

Baseline Tests	Interpretation/Action
If CD4 < 100, do Cryptococcal antigen (CrAg or CLAT) to test for Cryptococcus infection, and the need for fluconazole pre-emptive therapy	**If CLAT negative**: Start ART **If CLAT positive and asymptomatic**: Start Fluconazole 800 mg daily for 2 weeks, then fluconazole 400 mg daily for 2 months, followed by fluconazole 200 mg daily for a minimum of 1 year in total. Discontinue when patient has had two CD4 counts > 200 cells/μL taken at least 6 months apart; Start ART 2 weeks into antifungal treatment **If positive and symptomatic (symptoms include: headache, confusion)**: Refer to hospital urgently for lumbar puncture to exclude cryptococcal meningitis
Screen for HBV (HBsAg)	Start ART in patients with HBV co-infection, irrespective of CD4 count

Before starting	Interpretation/Action
TDF – Serum Creatinine (S_{Cr}) and eGFR/CrCl	To detect renal insufficiency. S_{Cr} is a waste product filtered by the kidneys. High levels in blood indicate impaired kidney clearance/function **If eGFR received from laboratory - use the value from the laboratory** > 50 mL/min: Can use TDF < 50mL/min: Use alternative, and investigate cause of renal dysfunction **No eGFR provided by laboratory and** Patient < 50 years AND not pregnant AND weighs > 50kg AND S_{Cr} < 100 μmol/L : Assume eGFR in acceptable range, and TDF can be used **No eGFR provided by laboratory and** Patient > 50 years OR weighs < 50 kg OR S_{Cr} > 100 μmol/L: Calculate CrCl using formula below
	Formula for non-pregnant adults (Modified Cockroft and Gault formula): $CrCl = \frac{(140 - age) \times Wt\ (kg)}{Scr\ (\mu mol/L)}$ * For females multiply the CrCl by 0.85
	Pregnant patient – eGFR can't be calculated, and the S_{Cr} is used to determine if TDF can be used: S_{Cr} < 85 μmol/L: Can use TDF S_{Cr} > 85 μmol/L: Use alternative and investigate cause of high S_{Cr}
AZT – Full blood count (FBC)/Hb	**To detect anaemia or neutropenia** – Hb > 8 g/dL: Can use AZT Hb < 8 g/dL: Use alternative
NVP – ALT	**To exclude liver disease** – ALT < 100 units/L: Can use NVP ALT > 100 units/L: Use alternative
LPV/r– Fasting cholesterol and TG	**To identify risk of LPV/r hyperlipidaemia** – Total cholesterol > 6 mmol/L – consider using ATV/r instead of LPV/r

Monitoring on ART

Remember to LOOK at results as soon as they come back from the laboratory and ACT on them as soon as possible

At every visit:
- Screen for TB, STI and pregnancy
- WHO Staging
- Ask about side effects

Test	Interpretation/Action
CD4 At 1 year on ART, and yearly if clinically indicated	To monitor immune response to ART, and eligibility for co-trimoxazole prophylaxis CD4 < 350: co-trimoxazole should be initiated/continued; patient should be on ART.
Viral load (VL) Month 6, 12 and then annually	**VL** – **Response** > 1000 – Address adherence, tolerability, drug-drug interactions, assess psychological issues and check Hb and HBsAg (if not done previously and TDF is part of first line) **On NNRTI-regimen**: Repeat VL 2 months later – if VL still > 1000: Consider switching to 2nd line 400 – 1000 – Assess adherence carefully. Repeat VL in 6 months, and manage accordingly < 400 – Repeat VL as per guideline

If on	Interpretation / Action
TDF S_{Cr} and eGFR at month 3,6,12 and then annually	eGFR > 60 mL/min: Continue TDF eGFR 50 – 60 mL/min: Continue on TDF, but do monthly eGFR for 3 months eGFR < 50 mL/min: Switch to alternative and investigate
AZT FBC at month 3, 6 and then annually	**Hb (g/dL) and Neutrophil count (× 10^9/L)** – **Action** Hb > 8 or Neutrophil > 1 – Continue AZT Hb < 8 or Neutrophil < 1 – Switch AZT to alternative Neutrophil < 1 – Stop co-trimoxazole
NVP ALT – only if rash OR symptoms of hepatitis develop e.g. Nausea, vomiting, abdominal pain, jaundice	ALT 40 – 100: repeat ALT in 2 weeks ALT 100 – 200: repeat ALT in one week* ALT > 200: Stop relevant drugs, do hepatitis screen and full LFT. INR should also be done in patients with jaundice * If symptoms of hepatitis or jaundice – stop relevant drugs, do hepatitis screen and full LFT. Do INR if patient is jaundiced
LPV/r Fasting cholesterol and TG at month 3	Fasting TG > 5 mmol/L: Switch to ATV/r Fasting total cholesterol > 6 mmol/L : Switch to ATV/r

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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Adult Dosage

Drug Name	Dosage	Dose adjustment in renal impairment	
		eGFR between 10 and 50 ml/min	eGFR < 10 ml/min
Abacavir (ABC)	300 mg twice daily OR 600 mg daily	Normal dose	Normal dose
Atazanavir + ritonavir (ATV/r)	300 mg/100 mg once daily	Normal dose	Normal dose
Darunavir + ritonavir (DRV/r)	600 mg/100 mg twice daily	Normal dose	Normal dose
Efavirenz (EFV) Swallow tablet whole	600 mg daily (or 400 mg if < 40 kg); usually given at night	Normal dose	Normal dose
Emtricitabine (FTC)	200 mg once daily	Not applicable	Not applicable
Etravirine (ETR)	200 mg twice daily	Normal dose	Normal dose
Lamivudine (3TC)	150 mg twice daily OR 300 mg once daily	150 mg daily	50 mg daily
Lopinavir + ritonavir (LPV/r) Swallow tablet whole	400 mg/100 mg twice daily NB: Patients on a rifampicin-containing TB regimen must have their dose increased to LPV/r 800/200 mg twice daily (See Table: Patients with concomitant TB)	Normal dose	Normal dose
Nevirapine (NVP)	200 mg daily for 2 weeks*, then 200 mg twice daily	Normal dose	Normal dose
Raltegravir (RAL)	400 mg twice daily	Normal dose	Normal dose
Stavudine (d4T)	30 mg twice daily	15 mg twice daily	15 mg daily
Tenofovir (TDF)	300 mg once daily	Avoid use	Avoid use
Zidovudine (AZT)	300 mg twice daily	Normal dose	300 mg daily

*Do not use nevirapine lead-in dose in patients already on rifampicin or if patient has been on efavirenz for more than 2 weeks; Do not increase the dose to 200 mg twice daily in the presence of a rash. Delay increase until rash stabilises or switch to alternative drug e.g. EFV

Patients with concomitant TB

Patients already on ART:
- Continue ART throughout TB treatment
- Efavirenz is the preferred agent in patients also on TB treatment. Patients on NVP, with no contraindication to EFV, should be switched to EFV
- Patients on LPV/r and rifampicin concomitantly should have their LPV/r dose doubled slowly over two weeks (to 800/200 mg twice a day). Monitor ALT while increasing the dose at weekly intervals, and then monthly while on double dose
- If patient on ATV/r containing regimen, then rifampicin should be replaced with rifabutin 150mg daily
- Patients requiring streptomycin/kanamycin/amikacin should avoid TDF, unless renal function is monitored weekly. AZT, d4T or ABC can be used in these patients. If need to continue TDF, due to Hepatitis B status, discuss the need for an aminoglycoside with a specialist
- Patients on third line ARVs should be discussed with an expert or the HIV hotline for management of drug interactions
- **Remember:** Patients on TB medication and ARVs are taking a large number of tablets. Do pre-emptive counselling to improve adherence

Patients not yet on ART:
- Patients who present with TB with a CD4 > 50 cells/μL, with no other serious HIV conditions (e.g. Kaposi's sarcoma or HIV encephalopathy) should start ART 8 weeks after starting TB treatment
- If patients need to start ARV therapy and are on rifampicin, and efavirenz is contraindicated, (e.g. psychosis or previous adverse reaction to efavirenz) start nevirapine, but do not use lead-in dose

Isoniazid preventive therapy (IPT)

Eligibility criteria:
- HIV positive AND
- Never had IPT before AND
- Active TB excluded

Contra-indications to IPT:
- Excessive alcohol use: Men > 28 units/week; women > 21 units/week
- Active TB disease
- Active liver disease
- Peripheral neuropathy
- History of adverse reactions to isoniazid
- Patients who completed MDR- or XDR-TB treatment

Dose of IPT:
- Isoniazid 300mg daily
- Vitamin B6 25mg daily

Adult patients who have completed TB treatment, where there is documented proof of bacteriological cure, can be started on IPT immediately, if they meet the above criteria
TST needs to be done to confirm duration of IPT. If TST is not available at initiation of IPT, then it should be done within ONE month of initiation of IPT

Duration of IPT:	TST not done	TST negative	TST positive
Pre-ART (regardless of CD4)	6 months	No IPT	36 months
Patients on ART	12 months	12 months	36 months

Management of treatment interruptions and defaulters

- Establish reason for default or treatment interruption
- Get a full history of previous treatment – what ARVs, duration of treatment, previous VLs
- If no history of previous documented failure, restart same regimen and do VL after 2 months
- If patient was on a NVP-containing regimen and interrupted > 1 week, restart with lead-in dose
- If patient has very low CD4, or is in the last trimester of pregnancy, or previously failed first line, but has not been started on second line and defaulted or interrupted treatment, consult with expert immediately or phone the HIV Hotline