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

WESTERN CAPE HIV TREATMENT GUIDELINES 2016

LATE ADOLESCENTS (> 15 YEARS) AND ADULTS

ELIGIBILITY AND TIMING OF ART

WHO IS ELIGIBLE TO START ART

All **HIV positive patients**, regardless of CD4 count or clinical staging

- Prioritise those with CD4 < 350 cells/mm³ or advanced HIV disease

PATIENTS REQUIRING FAST TRACKING

CD4 ≤ 200	Within 7 days
WHO stage 4 disease	Within 7 days
TB/HIV co-morbidity with CD4 < 50	Within 2 weeks of starting TB treatment
Pregnant or breastfeeding	Where capacity exists: initiate SAME day as eligibility established (otherwise within 7 days)

DELAY ART INITIATION IN THE FOLLOWING

ART delayed until treatment is tolerated, to allow improvement of symptoms, and prevent development of IRIS

Cryptococcal Meningitis (CM) prophylaxis (CLAT/CrAg +, **no** symptoms)	2 weeks after fluconazole treatment started
CM treatment (CLAT/CrAg + **plus** symptoms)	4-6 weeks on antifungal treatment
Tuberculosis (TB) with CD4 < 50	2 weeks on TB treatment
TB with CD4 > 50	2 - 8 weeks on TB treatment
TB meningitis	4-6 weeks on TB treatment

REGIMENS

1ST LINE

All **NEW PATIENTS**: • pregnant and breastfeeding women • adults (eGFR/CrCl > 50ml/min), with or without HBV or TB • adolescents > 15 years AND > 40 kg AND CrCl* > 80 mL/min	**TDF + FTC (or 3TC) + EFV** Provided as fixed dose combination (FDC)
Currently on **d4T**-based regimen: Change d4T to TDF if **virally suppressed** and eGFR**/CrCl > 50mL/min. If viral load (VL) > 1000, manage as potential treatment failure	**TDF** + FTC (or 3TC) + EFV FDC preferred
Adolescents currently 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

Contraindication to **EFV:** • Significant psychiatric co-morbidities **OR** • Intolerance to EFV **OR** • Where EFV may impair daily functioning e.g. shift workers	TDF + FTC (or 3TC) + **NVP**
Contraindication to **EFV and NVP** Don't use **NVP** if: • 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)	**ABC** + 3TC + EFV or (NVP)
Contraindication to **TDF and ABC** (previous hypersensitivity)	**AZT** +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 **ABC**-based 1st line regimen		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, fasting triglycerides > 5 mmol/L) OR gastrointestinal side-effects > 6 weeks on LPV/r OR cardiovascular event risk > 20% OR established clinical cardiovascular disease	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 genotyping resistance testing:

- Taking PI-based regimen for > 2 years, **AND**
- Viral load > 1000 on 3 separate occasions at least 2-3 months apart **AND**
- Patient adherent to treatment

MONITORING AT INITIAL DIAGNOSIS OF HIV

PARAMETER	PURPOSE & INTERPRETATION/ACTION
Confirm HIV status	To confirm HIV positive status in clients who present without documented proof of positive HIV status. Ensure that Western Cape testing algorithm has been followed
Baseline CD4 count and **WHO clinical staging**	Assess timing of ART and appropriate prophylactic treatment: CD4 < 200 – Initiate cotrimoxazole prophylactic treatment (CPT)
Pregnancy	Identify women eligible for ART, opportunity to offer appropriate family planning/conception
TB symptoms	Identify TB/HIV co-infection and timing of ART initiation with TB treatment
Mantoux / Tuberculin Skin Test (TST)	Assess need for Isoniazid prophylactic treatment (IPT) – see section on IPT
CrAg/CLAT if baseline **CD4 < 100**	**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
Other investigations: Screen for other STIs (sexually transmitted infections) and syphilis, major non-communicable diseases, measure weight (and height in adolescents)	

MONITORING PRIOR TO INITIATION OF ART

Serum creatinine (SCr) and **Creatinine clearance (CrCl)** if initiating **Tenofovir (TDF)**

To detect renal insufficiency
SCr is a waste product filtered by the kidneys used to determine eGFR/CrCl
If eGFR value is not provided by laboratory - calculate CrCl:

Adolescent < 16 years:

$$\text{CrCl}\left[\frac{\text{ml}}{\text{min}}\right] = \frac{\text{height [cm]}}{\text{serum creatinine [µmol/L]}} \times 40$$

Adult/adolescent > 16 years (non-pregnant):

$$\text{CrCl [ml/min]} = \frac{(140 - \text{age [years]})}{\text{serum creatinine [µmol/L]}} \times \text{weight [kg]}$$

Females: multiply CrCl x 0.85

If CrCl is **abnormal (< 60 ml/min):**
Check urine dipstix for proteinuria and repeat SCr after 1 month. Refer to specialist if renal dysfunction is persistent
Doses for ARVs may need to be adjusted for renal impairment
Tenofovir is contraindicated and should NOT be started in the following
eGFR/CrCl ≤ 50 ml/min in adults and adolescents > 16 years, or eGFR/ CrCl ≤ 80 ml/min in adolescents < 16 years
eGFR and CrCl cannot be calculated during **pregnancy.** If SCr ≥ 85 µmol/l don't use TDF and refer urgently

THE FOLLOWING TESTS SHOULD BE DONE IF FDC (TDF+FTC+EFV) CANNOT BE USED:

Haemoglobin (Hb) and **differential white cell count (WCC)** if initiating **Zidovudine (AZT)**	To detect anaemia/neutropenia **Hb > 8g/dL** – can use AZT **Hb ≤ 8g/dL** - do NOT use AZT (use alternative)
Alanine Transaminase (ALT) if initiating **Nevirapine (NVP)**	To detect liver dysfunction **ALT < 100 units/L** – can use NVP **ALT > 100 units/L** – discuss with specialist or call HIV & TB hotline
Fasting cholesterol and triglycerides if initiating **Lopinavir/ritonavir (LPV/r)**	To identify clients with contraindications to LPV/r or at risk of LPV/r related hyperlipidaemia **Cholesterol > 6mmol/L or triglycerides > 5mmol/L** – consider using atazanavir/ritonavir (ATV/r) instead of LPV/r

MONITORING ON ART

At every visit:

- Screen for TB, STI, pregnancy/planning to conceive and major non-communicable diseases
- Measure weight (and height in adolescents)
- Ask about side effects

TEST	PURPOSE & INTERPRETATION/ACTION
CD4 At 1 year on ART Repeat 12 monthly if CD4 < 200	To monitor immune response to ART, and eligibility for co-trimoxazole prophylaxis CD4 < 200: co-trimoxazole should be initiated/continued; patient should be on ART. If not, prioritise for initiation CD4 > 200 on two occasions at least 6 months apart: Stop monitoring, stop CPT and stop fluconazole prophylaxis
Viral load (VL) 1st line: Month 4, 12, then annually 2nd/3rd line: Month 6, 12, then annually On DR-TB treatment: Every 6 months until DR-TB treatment completed Pregnant/ breastfeeding: Refer to PMTCT guideline	VL: Response > 1000: Check adherence, tolerability, drug-drug interactions and assess psychological issues **On NNRTI-regimen**: Repeat VL 2 months later – if VL still > 1000: Check hepatitis B status (if not done previously and TDF is part of 1st line) and consider switching to 2nd line **On PI-based regimen**: Repeat VL after 6 months, and consider genotyping 400 - 1000: Assess adherence carefully. Repeat VL in 6 months, and manage accordingly < 400: Repeat VL as per guideline

IF ON	PURPOSE & INTERPRETATION/ACTION
TDF S_{Cr} and eGFR at month 1, 4, 12 and then annually	To detect TDF-toxicity See section on interpretation above
AZT FBC at month 1, 2, 3, and 6	To detect AZT toxicity Hb < 8g/dL – stop AZT and switch to alternative
On NVP or EFV and develops rash or symptoms suggestive of hepatitis **OR** **TB treatment and LPV/r** ALT	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, and annually if clinically indicated	TG > 5 mmol/L: Switch to ATV/r Total Cholesterol > 6 mmol/L : Switch to ATV/r Manage hyperlipidaemia with dietary modifications and appropriate statins if indicated (avoid simvastatin)
HBsAg Do test when switching off TDF	HBsAg positive: Continue TDF (see section on 2nd line) HBsAg negative: No need for TDF

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

DOSAGE

DRUG NAME	DOSAGE	DOSE ADJUSTMENT IN RENAL IMPAIRMENT	
		eGFR 10 -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
Dolutegravir (DTG)	No integrase inhibitor mutations: 50mg daily. If on rifampicin, use 50 mg twice daily Integrase inhibitor mutations present: 50 mg twice daily. If on rifampicin, avoid DTG	eGFR > 30: No dose adjustment; eGFR < 30: No data, use with caution	
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

PATIENTS WITH CONCOMITANT TB

Patients already on ART:

Continue ART throughout TB treatment
EFV-based regimens are generally preferred to NVP-based regimens in adolescents and adults with active TB on 1st line ART regimens
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 the patient is on an ATV/r containing regimen, then rifampicin should be replaced with rifabutin 150mg daily
Patients requiring streptomycin/kanamycin/amikacin avoid TDF, unless renal function is monitored weekly. AZT, d4T or ABC can be used in these patients.
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 2-8 weeks after starting TB treatment. If CD4 < 50, start ART within 2 weeks
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 PREVENTION THERAPY (IPT)

Eligibility criteria:	Contra-indications to IPT:	Dose of IPT:
• HIV positive **AND** • Never had IPT before **AND** • Active TB excluded	• Excessive alcohol use • Active TB disease • Active liver disease • Peripheral neuropathy • History of adverse reactions to isoniazid • Patients who completed MDR- or XDR-TB treatment	Isoniazid 300mg daily Vitamin B6 25 mg 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

Based on the Western Cape Consolidated Guidelines for HIV Treatment: Prevention of Mother-to-Child Transmission of HIV (PMTCT), Children, Adolescents and Adults. Western Cape Department of Health, South Africa. October 2016.

MEDICINES INFORMATION CENTRE

Western Cape Government Health

BETTER TOGETHER.

Published February 2017