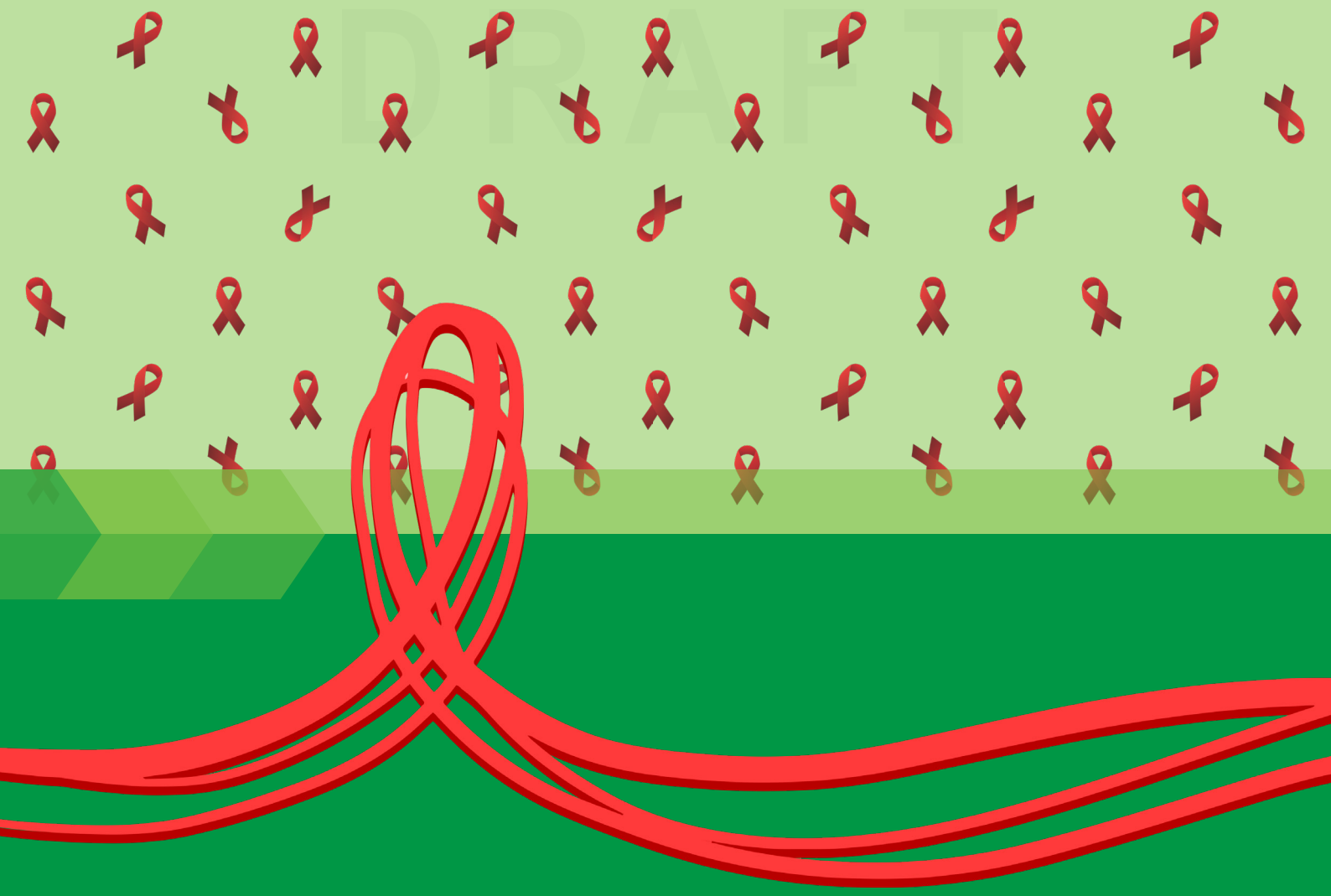


# 2023 ART Clinical Guidelines

## for the Management of HIV in Adults, Pregnancy, Adolescents, Children, Infants and Neonates

Draft 1: November 2022

Republic of South Africa National Department of Health

health

Department:
Health
REPUBLIC OF SOUTH AFRICA

2030 NDP

# Contents

## Foreword

South Africa is committed to attaining the UNAIDS 95-95-95 targets to control the HIV epidemic through quality comprehensive health services and use of highly effective antiretroviral treatment (ART). The principal goal of ART is to attain and maintain viral suppression, which will decrease morbidity and mortality from HIV as well as improve the quality of life for clients living with HIV.

The 2023 HIV clinical guidelines have been revised to increase access to the fixed dose combination (FDC) of Tenofovir (TDF) 300 mg + Lamivudine (3TC) 300 mg + Dolutegravir (DTG) 50 mg (TLD) for all eligible adults, adolescents and children over the age of 10 years and weighing 30 kg or more. This document intends to serve as a quick reference guide and job aid for healthcare workers. It intends to:

- Provide guidance on initiating naïve clients on DTG-containing regimens
- Provide guidance on switching existing clients on ART to DTG-containing regimens
- Provide guidance on supporting adherence and retention in care
- Highlight critical areas for the provision of integrated ART, TB and family planning services

The advantages of DTG is that it has a high genetic barrier to resistance, minimal side effects and drug interactions, and provides rapid viral suppression. It is well tolerated by patients and expected to contribute positively to adherence and retention on ART.

Implementation of these guidelines will increase access to ART services, advance South Africa's ability to control the epidemic and help to achieve the 2030 SDG goals.

I would like to thank all the internal and external stakeholders who actively contributed to the development of these guidelines.

It is our sincere wish that clinicians at all health care facilities across the board will use these guidelines to offer quality, comprehensive services to the public.

Dr Nicholas Crisp
Acting Director General: Health

## Overview

This ART Clinical Guideline is intended to serve as a quick reference guide for antiretroviral treatment (ART) in adults, pregnant women, adolescents and paediatric clients, and as a job aide for healthcare workers and implementing partners. This document is not intended to be exhaustive; for more information or details on any recommendations, or on the prevention of vertical transmission, please refer to the comprehensive Consolidated HIV Guidelines document and the Guideline for Family -Centred Transmission Prevention of Communicable Infections (HIV, Hepatitis, Listeriosis, Malaria, Syphilis and TB) 2023.

**The objectives of this document are to:**

- Provide guidance on initiation of ART in antiretroviral-naïve clients as well as those returning to care in the era of dolutegravir (DTG)
- Provide guidance for switching of clients already on ART to DTG-containing regimens
- Highlight critical areas for provision of integrated ART, TB, and family planning services.

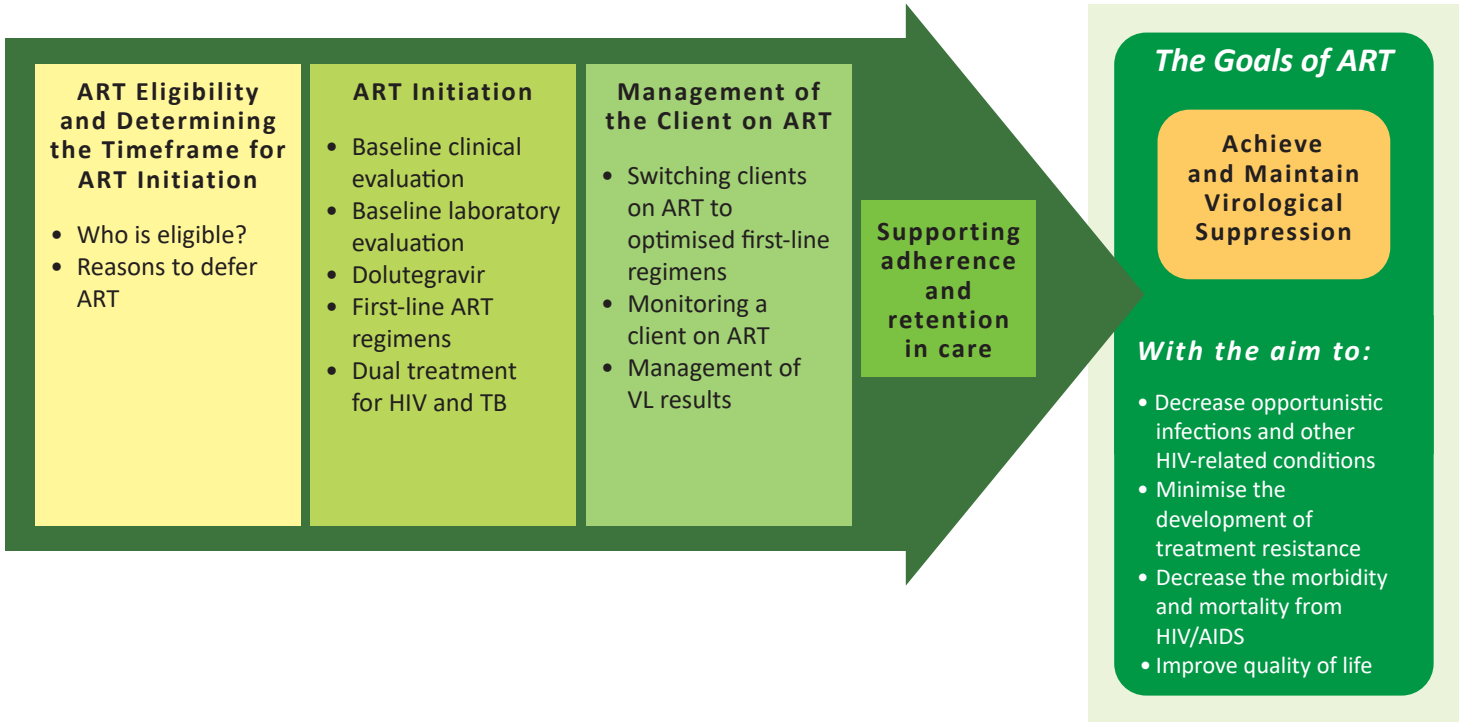
All people either currently on ART, or newly initiated on ART, should be screened for TB and assessed for TB preventive therapy (TPT) as indicated.

The preferred first-line ART regimen is tenofovir disoproxil fumarate-lamivudine-dolutegravir (TLD) for those clients initiating ART. The safety of DTG in women of childbearing-potential has been firmly established and neural tube defects are no longer a concern that influences regimen choice in women. However, the integration of family plan and ART services remain of paramount importance, and issues of family planning and contraception should be discussed at every clinical interaction to understand the client's current fertility desires and healthcare needs.

The guideline broadly follows the process of care, namely:

1) ART eligibility and determining the timeframe for ART initiation
2) ART initiation
3) Management of the client on ART
4) Supporting adherence and retention in care.

### *The Goals of ART*



## ART Eligibility

All people living with HIV (PLHIV) are eligible to start ART regardless of age, CD4 cell count and clinical stage.
For all clients without contra-indications, ART should be initiated within 7 days, and on the same day if possible. Pregnant women, infants and children under five years, and clients with advanced HIV disease should be prioritised for rapid initiation. Certain clients (including pregnant women) may be able to initiate ART on the same day as their HIV diagnosis, provided that they are clinically well, and are motivated to start ART. While rapid, and same-day where possible, initiation is encouraged, all clients, particularly those with advanced HIV disease, should be carefully assessed for opportunistic infections that may necessitate ART deferral.

### *Medical Indications to Defer ART*

| Medical Indications to Defer ART | |
|---|---|
| **Indication** | **Action** |
| TB symptoms (cough, night sweats, fever, recent weight loss) | Investigate for TB before initiating ART. If TB is excluded, proceed with ART initiation and TB preventive therapy (after excluding contra-indications to TPT). If TB is diagnosed, initiate TB treatment and defer ART. The timing of ART initiation will be determined by the site of TB infection and the client's CD4 cell count |
| Diagnosis of drug-sensitive (DS) TB at a non-neurological site (e.g. pulmonary TB, abdominal TB, or TB lymphadenitis) | Defer ART initiation as follows:<br>• If CD4 < 50 cells/µL – initiate ART within 2 weeks of starting TB treatment, when the client's symptoms are improving, and TB treatment is tolerated<br>• If CD4 ≥ 50 cells/µL – initiate ART 8 weeks after starting TB treatment |
| Diagnosis of drug-resistant (DR) TB at a non-neurological site (e.g. pulmonary TB, abdominal TB, or TB lymphadenitis) | Initiate ART after 2 weeks of TB treatment, when the client's symptoms are improving, and TB treatment is tolerated |
| Diagnosis of DS-TB or DR-TB at a neurological site (e.g. TB meningitis or tuberculoma) | Defer ART until 4-8 weeks after start of TB treatment |
| Signs and symptoms of meningitis | Investigate for meningitis before starting ART |
| Cryptococcal antigen (CrAg) positive in the absence of symptoms or signs of meningitis | Defer ART until the first 2 weeks of fluconazole prophylaxis has been completed |
| Confirmed cryptococcal meningitis | Defer ART until 4-6 weeks of antifungal treatment has been completed |
| Other acute illnesses e.g. *Pneumocystis jirovecii* pneumonia (PJP) or bacterial pneumonia | Defer ART for 1-2 weeks after commencing treatment for the infection |
| Clinical symptoms or signs of liver disease | Confirm liver injury using ALT and total bilirubin levels. ALT elevations > 120 IU/L with symptoms of hepatitis, and/or total serum bilirubin concentrations > 40 µmol/L are significant. Investigate and manage possible causes including hepatitis B, drug-induced liver injury (DILI), or alcohol abuse |
| Note: Clients who are already on ART should NOT have their treatment interrupted upon diagnosis of the above conditions | |

## ART Initiation

A clinical assessment and laboratory baseline investigations should be done in order to initiate ART. However, laboratory results do not need to be available to start clients on ART on the same day, provided they have no clinical evidence of TB, meningitis or renal disease. In addition, all clients, and caregivers of paediatric clients, must receive counselling on how to administer medication, monitor side-effects and deal with challenges to adherence.

### *Baseline Clinical Evaluation for Adults and Adolescents, Pregnant Women, and Children < 10 years*

The baseline clinical evaluation of a client about to start ART requires a thorough **history and clinical examination**. The minimum components of the baseline clinical evaluation are outlined in the table below.

| Component of the Baseline Clinical Evaluation | Purpose | Further Action Required | | |
|---|---|---|---|---|
| | | Adolescents (10-19 years) and Adults | Pregnant Women | Children (< 10 years) |
| **Recognise the client** with respiratory, neurological, or abdominal **danger signs needing urgent care** | To identify opportunistic infections and conditions needing urgent care or referral | Identify respiratory, neurological, or abdominal danger signs as outlined in Adult Primary Care (APC) guideline | Identify danger signs as outlined in the Maternity Care guidelines | Identify danger signs as classified in the IMCI Chart booklet |
| **Nutritional Assessment** | To identify recent weight loss that may indicate an active opportunistic infection (OI) or other pathology.<br>To identify underweight/ obese clients requiring nutritional and lifestyle support | Measure weight and height and determine BMI (kg/m$^2$):<br>< 18.5 = underweight;<br>18.5 to 25 = normal;<br>> 25 to < 30 = overweight;<br>≥30 = obese | Measure mid upper arm circumference (MUAC)<br>Women with MUAC < 23 cm require additional nutritional support/ referral | Plot weight, height and head circumference (if < 2 years) on growth chart, and measure MUAC to identify moderate and severe malnutrition |
| **Screen for TB** | To identify clients with a positive TB screen who require further investigations for TB<br>To identify clients with a negative TB screen who may be eligible for TPT (see page 7) | Identify symptoms of cough, night sweats, fever, recent weight loss as outlined in the TB screening tool | Do a TB symptom screen and **TB GeneXpert** for all HIV-positive women at first visit in antenatal clinic, due to the lower sensitivity of the TB symptom screen in pregnant women | Identify symptoms of cough, night sweats, fever, recent weight loss as outlined in the TB screening 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.** With cryptococcal meningitis, clients may only present with a recurrent headache. Other symptoms may include fever, neck stiffness or coma. Refer the client for a **lumbar puncture**. Defer ART if meningitis is confirmed as outlined in "Medical Reasons to Defer ART" on page 3 | | |

| Component of the Baseline Clinical Evaluation | Purpose | Further Action Required | | |
|---|---|---|---|---|
| | | Adolescents (10-19 years) and Adults | Pregnant Women | Children (< 10 years) |
| Screen for active depression, other **mental health** issues or substance abuse | Mental health conditions and substance use can affect adherence and the clients quality of life. In general, ART can be initiated, and cautiously monitored. (See also Annexure 3: Mental Health Assessment on page 22) | Screen for symptoms of depression, psychosis, and substance abuse | | Screen for symptoms of depression in older children |
| Screen for major chronic **non-communicable diseases (NCDs)** (diabetes, hypertension, epilepsy) | To identify and manage clients with major chronic NCDs and/or comorbidities.<br><br>To identify and prevent potential drug interactions with ART e.g. metformin and anti-epileptic medications | Do blood pressure (BP), and urine dipstix for proteinuria and glucose. Identify other risk factors (smoking, increased waist circumference, age) and determine cardiovascular (CVS) risk. Manage NCDs and CVS risk factors as outlined in the PHC EML | Do blood pressure (BP), and urine dipstix for proteinuria and glucose | Identify the child with epilepsy and be aware of potential drug interactions of anti-epileptic treatment and ART |
| Screen for **pregnancy** and ask if planning to conceive | To identify pregnancy and facilitate early referral for antenatal care (ANC) and measures to prevent mother-to-child transmission (MTCT).<br>To assess fertility intentions and contraceptive needs if not pregnant. | Ask if the client is currently using contraception and if her last menstrual period occurred at the expected time. If she answered "no" to either question, do a urine pregnancy test | N/A | N/A |
| Symptom screen for **sexually transmitted infections** (STIs) | To identify and treat STIs in sexually active clients | STI screening should include the following three questions:<br>"Do you have any genital discharge?"<br>"Do you have any genital ulcers?"<br>"Has/have your partner(s) been treated for an STI in the last 8 weeks? | | N/A |
| **Neurodevelopmental screen** | To identify children with neurodevelopmental delay requiring intervention/referral and follow-up | N/A | N/A | Screen for developmental delays as outlined in the child's Road to Health Booklet (RTHB) |
| **WHO clinical stage** | **After the baseline clinical evaluation has been completed by means of a thorough history and clinical examination, the client's WHO clinical stage can be determined:**<br><br>**At ART initiation**, WHO clinical stage helps us to:<br>Understand the severity of the client's clinical condition and the associated risk of mortality<br>Determine the urgency and timing of ART initiation<br>Determine if cotrimoxazole prophylaxis (CPT) is indicated (see "Indications for CPT" on page 7) | | | |

## *Baseline Laboratory Evaluation for Adults and Adolescents, Pregnant Women, and Children includes the following:*

The following baseline laboratory investigations should be performed routinely before a client initiates ART. Clients are not required to wait for the results of the baseline investigations prior to starting ART, but results should be checked at the next visit.

| Laboratory evaluation | Purpose | Adolescents (10-19 years) and Adults | Pregnant Women | Children (< 10 years) |
|---|---|---|---|---|
| **Confirm HIV test result** | To confirm HIV status for those without documented HIV status | ✓ | ✓ | ✓ |
| **CD4 cell count/ %** | To identify eligibility for CPT | See "Indications for starting and stopping cotrimoxazole" in table on page 7 | | |
| | To identify eligibility for cryptococcal antigen (CrAg) screening | A reflex CrAg test will be done automatically by the laboratory on all CD4 counts < 100 cells/µL | | N/A |
| **Creatinine and eGFR if TDF used** | To assess renal insufficiency | See table titled "**Assessing Renal Function**" on page 7 | | N/A |
| **Haemoglobin (Hb)** | To identify and manage anaemia; to determine eligibility for zidovudine (AZT) where necessary | If Hb is low, do a full blood count (FBC). Characterise according to mean corpuscular volume (MCV) as either microcytic, normocytic, or macrocytic and manage accordingly[1] | Treat with ferrous sulphate tds if Hb < 10 g/dL.<br>Refer if < 8 g/dL and symptoms, if anaemia diagnosed at 36 weeks gestation or later, or if no response to treatment | Children < 5 years: Treat with iron supplements and deworm the child[1]<br>Children > 5 years: Do FBC. Characterise according to MCV and manage accordingly[1] |
| **GeneXpert** | To diagnose TB | Only for those clients with a **positive TB symptom screen** | **Regardless of TB symptoms**, routinely do a TB GeneXpert for all HIV-positive women at first visit in antenatal clinic, due to the lower sensitivity of the TB symptom screen in pregnant women | Only for those with a **positive TB symptom screen** |
| **Cryptococcal antigen test (CrAg) if CD4 < 100 cells/ µL** | To identify asymptomatic clients who need pre-emptive fluconazole treatment | A reflex CrAg test will be done automatically by the laboratory on all CD4 counts < 100 cells/µL<br>If CrAg-negative, no fluconazole is required<br>If CrAg-positive, the client will require treatment of the infection<br>All CrAg-positive clients should be referred for a lumbar puncture, regardless of symptoms | All pregnant women with a positive CrAg should be referred for a lumbar puncture, regardless of symptoms. The results of the lumbar puncture and further management should be discussed with an expert, or one of the helplines provided on page 18 | N/A |
| **Cervical cancer screening** | To identify women with cervical lesions and manage appropriately | All HIV-positive women should be screened for cervical cancer at diagnosis and subsequently every 3 years if the screening test is negative. If positive, she should be referred for colposcopy and further interventions | Pregnancy does not preclude screening for cervical cancer and it can be performed up to 20 weeks of gestation. However, pap smear results may be more difficult to interpret in pregnancy, and any abnormal smears should be repeated at 6 to 12 weeks after delivery. | N/A |
| **HBsAg** | To identify those co-infected with hepatitis B (HBV) | If positive, exercise caution in stopping TDF-containing regimens, to prevent hepatitis flares | | N/A |

[1] As outlined in the PHC EML 2018

| Assessing Renal Function | | | | |
|---|---|---|---|---|
| | **Age/pregnancy Status** | **What must be measured?** | **Acceptable level for TDF use** | **Counahan Barratt formula**<br>eGFR (mL/min/1.73 $m^2$) = $\frac{\text{height [cm]} \times 40}{\text{creatinine [µmol/L]}}$ |
| | ≥ 10 and < 16 years of age | eGFR using Counahan Barratt formula | > 80 mL/min/1.73 $m^2$ | |
| | Adults and adolescents ≥ 16 years | eGFR using MDRD equation[1] | > 50 mL/min/1.73$m^2$ | |
| | Pregnant women | Absolute creatinine level | < 85 µmol/L | |

[1] Modification of Diet in Renal Disease Study (MDRD) equation. The MDRD formula is automatically calculated by the laboratory for those 18 years and older. For assistance in manually calculating the eGFR for adolescents between 16 and 18 years of age, please contact one of the helplines provided on page 18. Alternatively, use the calculator provided at https://www.mdcalc.com/mdrd-gfr-equation, or one of numerous smartphone applications available for this purpose. Ensure that the website/application uses the correct unit of measurement (i.e. µmol/L) for the creatinine level

## *Indications for Starting and Stopping Cotrimoxazole Preventive Therapy (CPT)*


| Age and HIV status | When to Start | When to Stop |
|---|---|---|
| HIV-positive infant under 1 year of age | All children under 1 year should be on cotrimoxazole irrespective of CD4% or clinical stage | |
| HIV-positive child 1-5 years of age | CD4% ≤ 25 %, WHO Stage 2, 3, and 4 | Discontinue if CD4 count > 25 %, regardless of clinical stage |
| HIV-positive child under 5 years of age with PJP infection | Start CPT after PJP treatment is completed | Continue CPT until 5 years of age and stop thereafter only if CD4 criteria in the older-than-five category are met |
| HIV-positive adults and children older than 5 years | CD4 count ≤ 200 cells/µL, WHO Stage 2, 3 and 4 | Discontinue if CD4 count > 200 cells/µL, regardless of clinical stage |

## *TB Preventive Therapy*

All clients starting ART, or already on ART, and who have not yet received TB Preventive Therapy (TPT), should be considered for TPT. Prior to initiating TPT, active TB should be ruled out by screening for TB symptoms. A Tuberculin skin test (TST) is not required prior to starting TPT.

| Category of Client | Specific Eligibility Criteria | Treatment and Duration |
|---|---|---|
| Adult or adolescent > 15 years (non-pregnant) | Any CD4 count. Exclude active liver disease, alcohol abuse, or known hypersensitivity to isoniazid | Isoniazid, oral, 300 mg daily for 12 months and pyridoxine 25 mg daily |
| Children who are contacts of index TB cases | Children < 5 years (regardless of HIV status), and children 5-14 years who are HIV-positive | Isoniazid, oral, 10 mg/kg/day for 6 months (maximum dose 300 mg daily) and pyridoxine daily |
| Pregnant women | Eligible if CD4 count ≤ 350 cells/µL. If CD4 > 350 cells/uL, defer TPT till 6 weeks after delivery* | Isoniazid, oral, 300 mg daily for 12 months and pyridoxine 25 mg daily |

* The APPRISE randomised control trial found a higher incidence of adverse pregnancy outcomes in mothers who used TPT in pregnancy

## Dolutegravir

### Dolutegravir (DTG) Overview

For further detail on switching **existing stable clients on ART** between regimens, see **"Switching existing clients to DTG-containing regimens"** on page 13

**Class of ARV:** Integrase Inhibitor (InSTI)

**Benefits:** DTG is a potent antiretroviral that provides rapid viral suppression, has a high genetic barrier to resistance, and has minimal side effects and drug interactions. It is well tolerated by patients and contributes positively to adherence and retention on ART.

**Formulations:**
- Fixed-dose combination: tenofovir (TDF) 300 mg + lamivudine (3TC) 300 mg + DTG 50 mg (TLD). TLD can be prescribed for clients ≥ 30 kg and ≥ 10 years of age
- DTG 50 mg tablet

**Standard Dose:** Children ≥ 20 kg; adolescents and adults: DTG 50 mg daily
Children > 4 weeks of age and 3-19 kg: As per paediatric dosing chart on page 24

**DTG dose with concomitant TB treatment:** Double DTG dose to 50 mg 12-hourly. If on TLD FDC, add DTG 50 mg 12 hours after TLD dose

**Side-effects:** Usually mild and self-limiting. Side-effects include insomnia, headache, central nervous system (CNS) effects, and gastrointestinal effects. DTG is known to decrease tubular secretion of creatinine without affecting glomerular filtration. Serum creatinine levels increase early in treatment (by less than 15%), remain stable throughout therapy, and are not an indication to stop DTG. A creatinine level that keeps on rising, is however a cause for concern and could indicate TDF toxicity or other underlying pathology. DTG can be taken in the evening or the morning as per the client's preference. However, if the client develops insomnia, TLD should be taken in the morning. recommended for all women who do not currently wish to become pregnant.

### Drug Interactions with Dolutegravir

! Drug interactions can result in suboptimal drug levels which can cause
- an elevated viral load
- drug resistance, due to replicating virus in the presence of subtherapeutic drug levels

| Interacting Drug | Effect of Co-Administration | Recommendation |
|---|---|---|
| Rifampicin | ↓ Dolutegravir | Double DTG dose to 50 mg 12-hourly.<br>If on TLD FDC, add DTG 50 mg 12 hours after TLD dose |
| Polyvalent cations ($Mg^{2+}$, $Fe^{2+}$, $Ca^{2+}$, $Al^{3+}$, $Zn^{2+}$) e.g. antacids, sucralfate, multivitamin and nutritional supplements | ↓ Dolutegravir | Calcium supplements decrease DTG concentrations if taken together on an empty stomach. To prevent this, DTG and calcium supplements can be taken at the same time if taken with food.<br>Iron supplements decrease DTG concentrations if taken together on an empty stomach. To prevent this, DTG and iron supplements can be taken at the same time if taken with food. However, calcium and iron supplements must be taken at least 4 hours apart.<br>Magnesium/aluminium containing antacids decrease DTG concentrations regardless of food intake and should be taken a minimum of 2 hours after or 6 hours before DTG |
| Anticonvulsants:<br>• Carbamazepine<br>• Phenobarbital<br>• Phenytoin | ↓ Dolutegravir | Avoid coadministration if possible. Alternative agents that do not interact with DTG include valproate, lamotrigine, levetiracetam, and topiramate. Double DTG dose to 50 mg 12-hourly for carbamazepine, phenytoin, or phenobarbital if an alternative anticonvulsant cannot be used |
| Metformin/DTG | ↑ Metformin | DTG increases metformin levels.<br>Maximum metformin dose 500 mg 12-hourly |

! This table includes some of the most important drug interactions with DTG. Note that efavirenz, lopinavir/r and atazanavir/r also have important drug interactions. For more information, please refer to the following resources: *www.hiv-druginteractions.org/checker*, the Liverpool HIV iChart application for smart phones, or any of the helplines provided on page 18

## All Adult and Adolescent Females and Males ≥ 30 kg and ≥ 10 years of Age

TDF + 3TC + DTG (TLD)

## Neonates, Infants and Children 0 to < 10 years of Age

| 2.0 kg | Birth to < 4 weeks of age[1] | 3 kg | ≥ 4 wks of age, to < 10 years of age | 30 kg | and ≥ 10 years of age |
|---|---|---|---|---|---|
| | Neonates AZT + 3TC + NVP | | Infants and Children ABC + 3TC + DTG | | Adults and Adolescents TDF + 3TC + DTG (TLD) |
| | For further details on initiating ART in term and pre-term neonates see pages 20-21 | | Transition does not require a VL before switching | | Transition does not require a VL before switching Ensure adequate renal function[2] |

For further detail on transitioning between regimens, see "Switching existing clients to DTG-containing regimens" on page 13-14

[1] For neonates with severe anaemia, obtain advice from an expert or through one of the helplines provided on page 18

[2] Before switching to TDF, ensure adequate renal function by checking eGFR/creatinine as outlined in table on page 7

## ART Initiation in Women and Adolescent Girls Diagnosed with HIV during Labour

During labour, give a stat single fixed-dose combination tablet of TLD and a stat single dose of nevirapine (NVP).

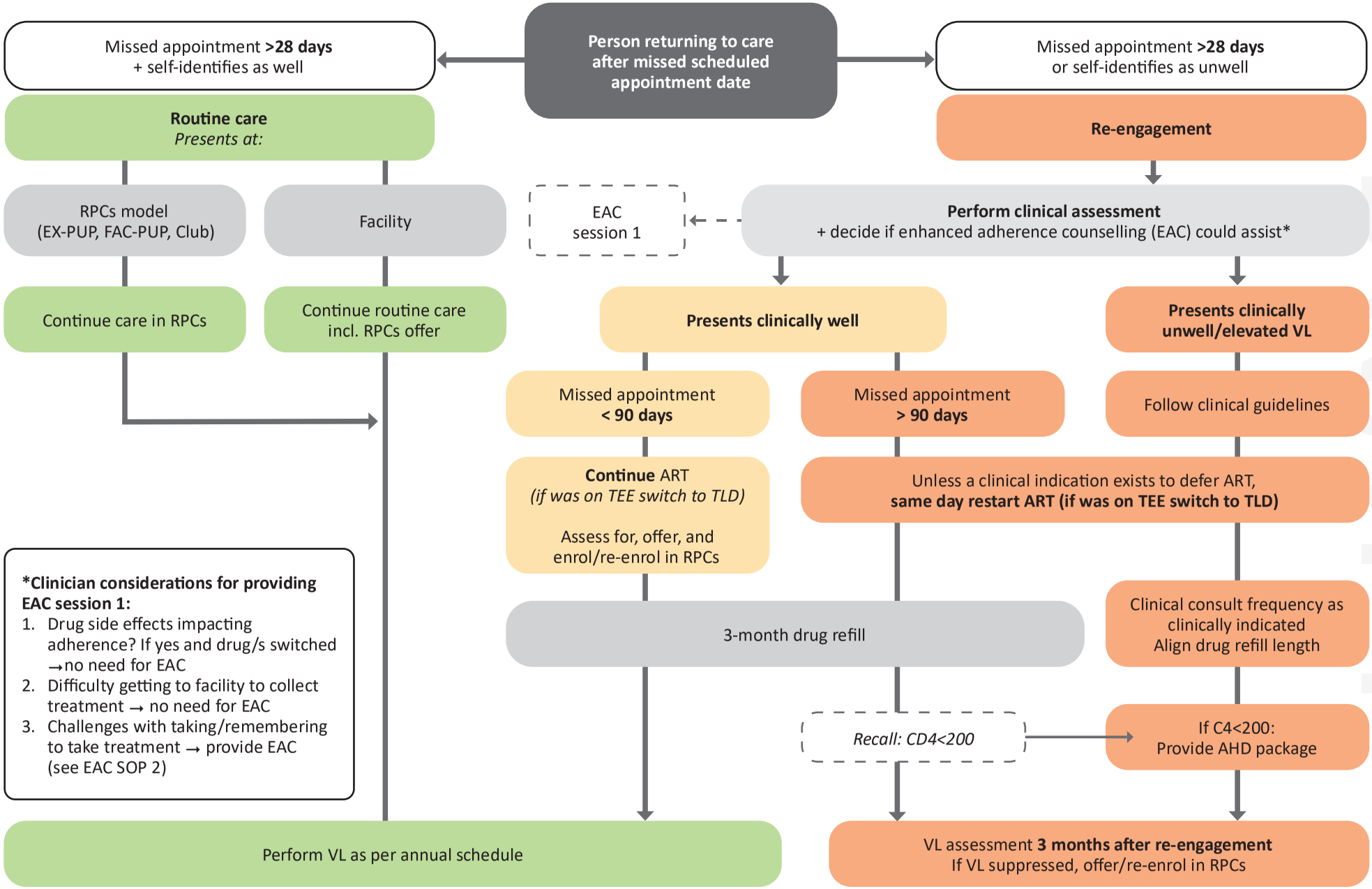
Lifelong ART should be initiated the following day. TLD and a contraceptive method is recommended. Provide her with a choice of contraceptive options as desired.

Appropriate ART literacy education should be given to the woman before she leaves the facility. Provide a 2-month supply of her chosen first-line ART regimen at discharge from labour ward.


Concerns regarding neural tubes defects (NTDs) on DTG in previous years created an important focus on the integration of family planning into ART services. Although evidence has shown that there is no increased risk for NTDs on DTG-containing regimens, family planning services should continue to be offered with ART services in an integrated and patient-centred manner.

Women should be **provided a choice of contraceptive options**, which includes condoms, oral contraceptives, implants, injectables, and intra-uterine contraceptive devices (IUCDs). Dual methods are recommended, and consist of a hormonal method or IUCD to prevent pregnancy, and a barrier method (male/female condoms) to prevent STIs and HIV transmission.

Contraceptive choices need to respect and fulfill human rights and enable clients to make informed choices for themselves. Client contraceptive choices, however, are often influenced directly or indirectly by social, economic and cultural factors. It is in this context that clients should be given comprehensive, scientifically accurate information in order to assist them to make an informed, voluntary choice of a contraceptive method.


Person returning to care after missed scheduled appointment date
Missed appointment >28 days + self-identifies as well
Missed appointment >28 days or self-identifies as unwell
Routine care
Presents at:
Re-engagement
RPCs model (EX-PUP, FAC-PUP, Club)
Facility
EAC session 1
Perform clinical assessment + decide if enhanced adherence counselling (EAC) could assist*
Continue care in RPCs
Continue routine care incl. RPCs offer
Presents clinically well
Presents clinically unwell/elevated VL
Missed appointment < 90 days
Missed appointment > 90 days
Follow clinical guidelines
Continue ART (if was on TEE switch to TLD)
Assess for, offer, and enrol/re-enrol in RPCs
Unless a clinical indication exists to defer ART, same day restart ART (if was on TEE switch to TLD)
3-month drug refill
Clinical consult frequency as clinically indicated
Align drug refill length
Recall: CD4<200
If C4<200: Provide AHD package
*Clinician considerations for providing EAC session 1:
1. Drug side effects impacting adherence? If yes and drug/s switched →no need for EAC
2. Difficulty getting to facility to collect treatment → no need for EAC
3. Challenges with taking/remembering to take treatment → provide EAC (see EAC SOP 2)
Perform VL as per annual schedule
VL assessment 3 months after re-engagement
If VL suppressed, offer/re-enrol in RPCs

TB/HIV co-infection impacts on ART in a number of ways. It affects:

1. **The timing of ART initiation** (see "Indications to defer ART" on page 3)
2. **Drug selection** in clients who are not yet on ART when TB treatment is initiated
3. Drug levels, due to significant **drug interactions** that reduce ART concentrations in the blood
4. **Adherence**, due to increased pill burden
5. **Side-effects** due to overlapping toxicities, e.g. hepatic toxicity

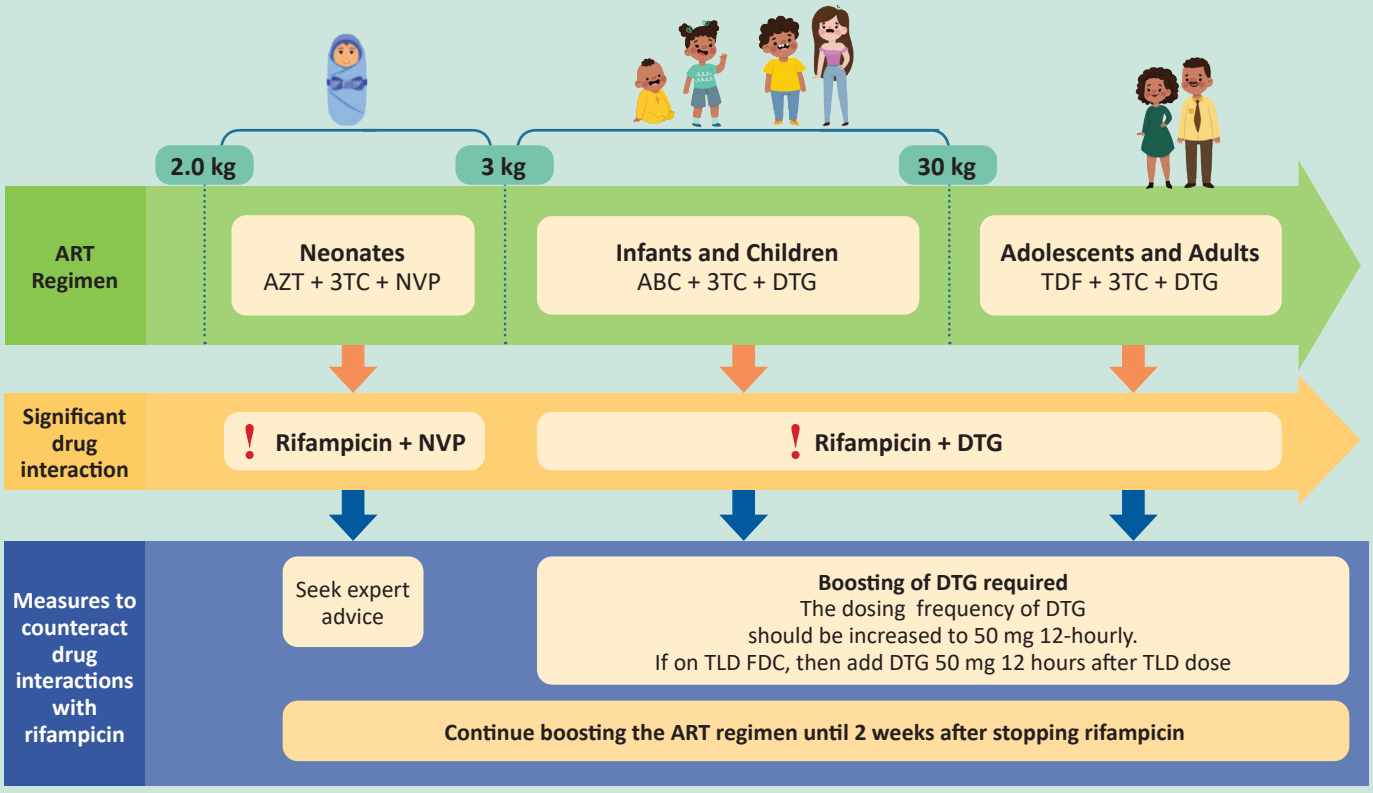
**Efavirenz** has no significant interaction with rifampicin

Adult clients **who are not yet on ART** when TB treatment is initiated should initiate ART with an EFV-containing regimen.
Adults who are **already on an EFV-containing regimen** when TB treatment is initiated should continue the EFV-containing regimen whilst also taking TB treatment.

In both these situations, the EFV-containing regimen should be continued until two weeks after TB treatment is completed. Thereafter, EFV can be switched to DTG.

## Drug Interactions

Rifampicin-containing TB treatment has significant drug interactions with all paediatric ART regimens, as well as with adult/adolescent regimens containing DTG:




### Drug Interactions with Lopinavir/ritonavir

Every effort should be made to switch children to DTG-containing regimens. However, during the transition process, some children may still be on PI-containing regimens and may also require TB treatment. Significant drug interactions between LPV/r and rifampicin should be managed as follows:

**LPV/r tablets: Double-dose LPV/r tablets**
(See Dosing Chart on page 24). Tablets can be used only if the child is able to swallow whole LPV/r tablets (tablet must not be crushed, broken or chewed).
If the child is unable to tolerate LPV/r at double doses, consult one of the helplines provided on page 18.
**LPV/r solution: Super-boosting** with additional ritonavir solution or ritonavir powder: maintain standard LPV/r dose but add additional ritonavir twice daily as per Dosing Chart on page 18. If no ritonavir solution or powder is available, consult an expert for a suitable alternative. Ritonavir solution has a shelf-life of only 6 months, whereas ritonavir powder has a shelf-life of 36 months. Note that ritonavir 100 mg tablets must not be crushed, broken or chewed.

## *Switching existing clients to DTG-containing regimens*

***(who have never used a DTG-containing regimen in the past)***

| **Non VL-dependent regimen switches**<br>Regimens where the VL result will not influence nor delay the decision to switch to a DTG-containing regimen | | | |
|---|---|---|---|
| **VL considerations** | **Current Regimen** | **Criteria for switch** | **Regimen if change indicated** |
| **Switching regardless of VL result** | **TEE**<br>ABC/3TC/EFV<br>AZT/3TC/EFV<br>AZT/3TC/DTG<br>Any LPV/r or ATV/r regimen for **less than 2 years** | **Switch all to a DTG-containing regimen, regardless of VL result**<br>Review VL in last 12 months.<br>If VL in last 12 months was not suppressed, continue to switch same day, but do ABCDE assessment and provide enhanced adherence counseling (EAC) if needed.<br>If VL was not done in last 12 months, do it at this visit, but do not wait for the result to switch | **TLD**<br>provided no renal dysfunction and age > 10 yrs and weight > 30 kg<br>If client does not qualify for TDF **ABC[1]/3TC/DTG**<br>If client does not qualify for TDF and has ABC hypersensitivity **AZT/3TC/DTG** |

| **VL-dependent regimen switches**<br>Relevant to all clients who have been on PI-based regimens for more than two years: their VL result in the last 12 months will influence the decision of how and when to switch to a DTG-containing regimen | | | |
|---|---|---|---|
| **VL considerations** | **Current Regimen** | **Criteria for switch** | **Regimen if change indicated** |
| **VL < 1000 c/mL** | **Any LPV/r or ATV/r regimen** for **more than 2 years** | **Switch all to a DTG-containing regimen**<br>If VL in last 12 months was not < 50 c/mL, continue to switch same day, but do ABCDE assessment and provide EAC if needed | **TLD**<br>provided no renal dysfunction and age > 10 yrs and weight > 30 kg<br>If clients does not qualify for TDF **ABC[1]/3TC/DTG** |
| **[2] Two or more VLs ≥ 1000 c/mL** taken **two or more years** after starting TLD regimen | Adult or adolescent on any **LPV/r or ATV/r** regimen for **less than 80%[3]** | **Switch all to a DTG-containing regimen**<br>**Do not do a resistance test**<br>These clients are unlikely to have PI resistance mutations. Rather switch to a more tolerable once daily FDC regimen which is likely to support adherence | **TLD**<br>provided no renal dysfunction and age > 10 yrs and weight > 30 kg<br>If clients does not qualify for TDF **ABC[1]/3TC/DTG** |
| | Adult or adolescent on any **LPV/r or ATV/r** regimen and adherence **more than 80%[3]** | Clients who meet the definition of confirmed virological failure despite confirmed adherence more than 80% may need a resistance test.<br>**These clients do not qualify for a same-day switch.**<br>Discuss with an HIV expert[4] to authorise and interpret a resistance test<br>Provide individualised regimen as recommended by HIV expert | |
| | Child < 10 years, or weight < 30 kg on any **LPV/r or ATV/r regimen** | These clients do not yet qualify for TLD and may require a resistance test.<br>Refer to algorithm<br>**"Switching children on PI-containing regimens to DTG-containing regimens"** on page 14 | |

1. If clients are not eligible to use TDF and they have ABC hypersensitivity, use AZT/3TC/DTG
2. Confirmed virological failure is defined as two or more VLs ≥ 1000 c/mL taken two or more years after starting a DTG or PI containing regimen, despite adherence > 80% by objective measurement. A patient who has only 1 VL > 1000 after 2 years on a PI-based regimen should have an ABCDE assessment, EAC if applicable, and their VL repeated in 3 months. The result of the repeat VL will allow the patient to be grouped into one of the categories in the table above and will inform the further course of action
3. Objective measures of good adherence include at least one of:
   - Pharmacy refills > 80% in the last 6-12 months (if this is known)
   - Attendance of > 80% of scheduled clinic visits in the last 6-12 months (if this is known)
   - Detection of current antiretroviral drug/s in the client's blood or urine, if available

   **Note:** Self-reported adherence is not considered a reliable measure of good adherence!
4. For advice from an HIV expert, approach an HIV Hotline, an infectious disease specialist, or the Third Line ART committee

## *Switching Children on PI-containing Regimens to DTG-containing Regimens*

**Child** (< 10 years, or weight < 30 kg) on a **PI-containing regimen**
*(who have never used a DTG-containing regimen in the past)*

On **PI** for at least **2 years**

On PI for **less than** 2 years, irrespective of VL

**Two** or more **VLs ≥ 1000** c/mL
taken two or more years after starting PI regimen

**VL < 1000 c/mL**

**Adherence < 80%** [1]

**Adherence < 80%** [1]

For children on LPV/r solution or pellets, consider switch to **4-in-1 ABC/3TC/LPV/r** capsules to improve tolerance/ adherence & **repeat VL** after 2-3 months

Children on other LPV/r formulations

**VL ≥ 1000 c/mL**

**VL < 1000 c/mL**

**Discuss with an HIV expert** [2]
to authorise and interpret
**a resistance test**

**Individualised regimen**
as recommended by HIV expert

**ABC + 3TC + DTG**

If the most recent VL before their regimen change was > 50 c/mL,
**repeat VL 3 months after starting the new regimen to confirm viral re-suppression**

1. Although objective measures of poor adherence include pharmacy refills or attendance attendance of scheduled clinic visits in the previous 6-12 months of <80%, adherence difficulties in young children are often linked to poor tolerability of unpalatable formulations, particularly LPV/r solution. It is important to ask the caregiver about how the child tolerates the medication e.g., does the child refuse to swallow the medicine or spit out or vomit the medicine, and whether the caregiver has been able to overcome this. Considering these limitations, objective measures of good adherence could include one of the following:
   a. Pharmacy refills > 80% in the last 6-12 months (if this is known)
   b. Attendance of > 80% of scheduled clinic visits in the last 6-12 months (if this is known)
   c. Detection of current antiretroviral drug/s in the client's blood or urine, if available mentioned above should be considered
2. The following would qualify as HIV experts: the HIV Helplines, a paediatric infectious disease specialist or the paediatric Third line ART committee

If in doubt about any aspect of viral load management or switching to second-line, contact one of the following resources:

National HIV & TB Health Care Worker Hotline: **0800 212 506**
Right to Care Adult HIV Helpline: **082 957 6698**
Right to Care Paediatric and Adolescent HIV Helpline: **082 352 6642**
KZN Paediatric Hotline: **0800 006 603**

## *Summary of the Care Continuum for Adult Clients on ART*

Clients on ART can be differentiated into those who are 1) clinically well and adherent on ART and 2) those who are clinically non-stable and/or struggling with adherence. Clients that are clinically well at their first clinical review return after starting ART, only need to be seen again 2 months later for clinical review and their first viral load. After that, taking treatment and clinical follow-up should be made as convenient as possible for the client. Therefore, they may continue to receive ART using a differentiated care approach, provided they meet the eligibility criteria of 1) having a suppressed VL, 2) being clinically well with no opportunistic infections (OIs), and 3) not being pregnant. The diagram below provides a summary of the components of care at different visits for clinically well and adherent clients during the first year on ART. Clients who are enrolled in RPCs should be rescripted for RPCs at their comprehensive clinical review at which a further VL will be taken. Clients should not be required to come back the following month for VL result review prior to rescript. Rather, recall to the facility only those clients with elevated VL. For more detail on repeat prescription strategies (RPCs), see the National Adherence Guideline standard operating procedures (SOPs) 5-7 (facility-pick-up points, adherence clubs and external pick-up points).

| Months On ART | VL monitoring | Overview of Management |
|---|---|---|
| 0 | ART initiation and session 1 of fast track initiation counselling | |
| 1 | | • Session 2 of fast track initiation counselling including planning for travel and VL education<br>• Clinical assessment and routine monitoring as outlined on page 15<br>• Integrated management for multiple chronic conditions<br>• **2 months ART dispensed (2MMD) - AGL SOP 4** |
| 3 | **3-month VL** | • Clinical assessment including VL and any other routine monitoring bloods as outlined on page 15<br>• Integrated management for multiple chronic conditions |
| 4 | **Month 4** | • Clinical assessment and review of VL and any other monitoring results<br>• Integrated management for multiple chronic conditions<br>• Assess eligibility for repeat prescription collection strategies (RPCs)<br>  • VL < 50 c/mL<br>  • Clinically well<br>  • No OIs<br>  • Not pregnant |
| | | Facility Pick-up Point (FAC-PUP) AGL SOP 5 / Adherence Clubs (AC) Facility or community-based support groups AGL SOP 6 / External Pick-up point (EX-PUP) AGL SOP7) |
| | | • Renew prescription for next 6 months, with first month's supply issued today from the facility<br>• If not eligible for RPCs or refused RPCs: Assess eligibility for facility provided multi-month dispensing (MMD) – AGL SOP 4 |
| 5 - 9 | **Month 5 onward** | • Collect medication from preferred RPCs |
| 10 | **10-month VL** | • Clinical assessment including VL and any other monitoring bloods<br>• Integrated management for multiple chronic conditions<br>• Renew prescription for next 6 months.<br>• Do not require the clients to return to the facility in 1 month to review the VL results. Rather, recall to the facility only those clients with elevated VLs |
| 11+ | **Month 11 onward** | • Collect medication from preferred RPCs<br>• Annual clinical assessment as outlined on page 15<br>• 12-monthly routine VL monitoring |

Stable and Adherent on ART

**Non-stable clients**

If at any stage the client becomes clinically non-stable and /or non-adherent i.e. a client who has:

- missed a scheduled appointment by more than 28 days (including in an RPCs)
- a VL > 50 c/ml
- possible signs or symptoms of treatment failure

A clinicians should:

- Assess the unstable client
- Provide appropriate clinical management
- If clinically well and struggling with visit frequency: provide multi-month dispensing (Adherence Guideline SOP 4)
- If experiencing side effects or the child cannot tolerate their medication: switch drugs/formulation
- If struggling to take ART as prescribed: enhanced adherence counselling (See Annexure 3)

*See also the Re-engagement algorithm on page 10*

! Do not turn away an ART client who reports to have run out of treatment and presents without a transfer letter!

## *Monitoring on ART*

Providing quality care at the follow-up visit is essential to promote adherence, achieve and sustain viral suppression, minimise side-effects and toxicities, and promote quality of life. A client on ART should be monitored to:

1. Determine clinical response to ART
2. Determine the virological and immunological response to ART
3. Detect and manage any side-effects and toxicities

### The following components should be included in the **clinical assessment:**

**Weight (adults)**
An assessment of trends in weight in adults

**Growth and neurodevelopment (children)**
An assessment of trends in weight, height, head circumference, and neurodevelopment

! Remember to adjust ART dosage according to weight!

**Screen for TB and other OIs:**
to diagnose and provide treatment;
to adjust ART regimen if required;
to determine if TB preventive therapy is required

**WHO clinical staging**
to determine response to ART, and CPT eligibility

**Screen for pregnancy and ask if planning to conceive** as outlined in the table for "Baseline Clinical Evaluation" on page 5

### **Viral load** should be measured to timeously detect problems with adherence or treatment failure

At month 3 on ART and month 12 on ART
Thereafter, if virally suppressed, repeat every 12 months

! Remember, an elevated VL is a medical emergency!
Assess and manage according to the "VL Monitoring for clients on TLD" algorithm on page 16

### **The CD4 count** should be measured to monitor susceptibility to opportunistic infections and eligibility for CPT

At month 12 on ART
Thereafter, repeat every 6 months until client meets criteria to discontinue CPT. Stop CD4 monitoring if client's VL remains below 1000 c/mL.
If VL >1000 c/mL, monitor CD4 count every 6 months.

### **Side-effects and ART toxicities** can affect adherence and endanger the client's health:

**Drug side-effects**
Ask about side-effects at each visit (e.g. sleep or gastrointestinal disturbances)

**TDF-induced nephrotoxicity**
If on TDF, do creatinine and eGFR* at months 3 and 12
Thereafter, repeat every 12 months

**Dyslipidaemia**
If on a PI-based regimen (ATV/r, DRV/r), do total cholesterol and triglycerides (TGs) at month 3
If above acceptable range, do fasting cholesterol and TGs and if still above acceptable range, obtain expert advice

**Anaemia and neutropaenia**
If on AZT, do a full blood count and differential white cell count at months 3 and 6
Thereafter, repeat if clinically indicated

### *Assessing Renal Function

| Age/pregnancy status | What must be measured? | Acceptable level for TDF use |
|---|---|---|
| > 10 and < 16 years of age | eGFR using Counahan Barratt formula | > 80 mL/min/1.73 $m^2$ |
| Adults and adolescents ≥ 16 years | eGFR using MDRD equation[1] | > 50 mL/min/1.73$m^2$ |
| Pregnant women | Absolute creatinine level | < 85 µmol/L |

**Counahan Barratt formula**

$$\text{eGFR (mL/min/1.73 m}^2\text{)} = \frac{\text{height [cm] x 40}}{\text{creatinine [µmol/L]}}$$

[1] Modification of Diet in Renal Disease Study (MDRD) equation. The MDRD formula is automatically calculated by the laboratory for those 18 years and older. For assistance in manually calculating the eGFR for adolescents between 16 and 18 years of age, please contact one of the helplines provided on page 18. Alternatively, use the calculator provided at https://www.mdcalc.com/mdrd-gfr-equation, or one of numerous smartphone applications available for this purpose. Ensure that the website/application uses the correct unit of measurement (i.e. µmol/L) for the creatinine level

## *VL Monitoring for Clients on TLD*

*(also applicable to other DTG-containing regimens)*

**Routine VL monitoring** at 3 months on ART, at 1 year (10-12 months) on ART, and 12-monthly thereafter

**VL < 50 c/mL**

VL unsuppressed (VL > 50 c/ml)
(This include previous VL level of 50-999 and VL > 1000 c/ml)

Do a thorough assessment of the cause of an elevated VL. Consider the possibility of:
A. **A**dherence problems *(see page 17)*
B. **B**ugs (Intercurrent infections)
C. In-**C**orrect ART dosage *(see Annexure 5)*
D. **D**rug Interactions *(see page 9)*
E. R**E**sistance (if > 2 years on treatment)

**Implement interventions to re-suppress the VL**, including **Enhanced Adherence Support** if indicated
(See Annexure 3 Enhanced Adherence Counselling)
Recommend **condom use and contraception** as appropriate

Repeat VL after 3 months

Repeat VL **unsuppressed** [1] **(VL > 50 c/ml)**

**Re-assess and resolve adherence issues!** [2]
*(See "Assessing an elevated VL" on page 17 and Annexure 3 Enhanced Adherence Counselling)*

On TLD for **at least 2 years**

On TLD **less than** 2 years [3]

If **Adherence > 80%** [4], and
**Two** or more **VLs ≥ 1000 c/mL**
taken two or more years after starting TLD regimen
or at least one VL ≥ 1000 c/mL and either
CD4 < 200 cells/mm3 or an opportunistic infection

If adherence still
suboptimal [4],
or persistent low-level viraemia
(2 or more consecutive VLs between
50 and 999 c/mL)

Go to the algorithm for
**"Management of confirmed virological failure on TLD"** on page 18

**Repeat VL at next scheduled routine VL**
(i.e., in 6 months', time)
Intensify efforts to **resolve adherence issues** [2]

1. Due to their high genetic barrier, resistance to a first-line DTG-containing (TLD1) regimen is extremely rare. If other reasons for an unsuppressed VL have been addressed or excluded, e.g., drug interactions, and the client remains unsuppressed at their repeat VL, suboptimal adherence remains the most probable cause for non-suppression. The highest probability of improving adherence would be to remain on a once-daily, well-tolerated, fixed-dose combination regimen (TLD) while identifying and addressing the underlying root causes of non-adherence. 99,9% of these clients will re-suppress on TLD if adherent!
2. Repeat ABCDE assessment as outlined on page 17. Remember to ask about treatment side-effects, the potential cost of transport or loss of income related to clinic visits, mental health conditions, and current or prior drug interactions. Current or previous drug interactions with rifampicin, carbamazepine, phenytoin, phenobarbital, or the polyvalent cations may have resulted in the development of resistance.
3. Drug interactions may also warrant an expert discussion and authorisation of a resistance test earlier than 2 years on the regimen. If necessary, discuss with an expert
4. Objective measures of good adherence include at least one of:
   a. Pharmacy refills > 80% in the last 6-12 months (if this is known)
   b. Attendance of > 80% of scheduled clinic visits in the last 6-12 months (if this is known)
   c. Detection of current antiretroviral drug/s in the client's blood or urine, if available

   **Note:** Self-reported adherence is not considered a measure of good adherence!

ART, Antiretroviral therapy; DTG, Dolutegravir; LLV, Low-level viraemia; SOP, Standard operating procedure; TL, Third-line; TLD, fixed-dose combination of tenofovir, lamivudine, DTG; VL, Viral load.

## *Assessing and Elevated Viral Load*

> **!** Do not turn away an ART client who reports to have run out of treatment and presents without a transfer letter!

| A thorough assessment is essential for any client with a viral load measuring ≥ 50 c/ml | | | |
|---|---|---|---|
| Adherence | A | Is adherence to medication poor?<br>Ask about factors that may influence adherence e.g.<br>• Direct cost of clinic visits to patient, e.g. transport, loss of income, cost of paying another person to take on social responsibilities<br>• Taking time away from existing work, finding work and/or social care responsibilities<br>• Needing to travel for extended periods of time<br>• Medication side-effects<br>• Unpalatable medications<br>• Depression<br>• Alcohol or substance abuse<br>• Poor social support<br>• Non-disclosure<br>Pregnant women may experience nausea, heartburn, and constipation. Assess the need for symptomatic treatment with an anti-emetic, anti-diarrhea agent, or fiber supplement. | **Tips**<br>Ask open ended questions e.g. "What makes it difficult for you to take your treatment?", and "How many doses have you missed this week?"<br>Be non-judgemental. Statements like "we all miss a dose now and then" can encourage a client to be more open. |
| Bugs | B | Check for symptoms and signs of infection.<br>Do a TB and STI screen. | Remember that immune compromised, malnourished, and pregnant clients may not exhibit overt symptoms of TB. If in doubt, do a TB GXP. |
| Correct Dose | C | Is the client on the correct dose for their weight?<br>This is especially applicable to growing children, or clients with previous renal impairment. | |
| Drug | D | Are there any potential drug interactions? Consider:<br>• Other prescribed treatment e.g. rifampicin, anti-epilepsy drugs<br>• Over the counter treatment e.g. antacids<br>• Supplements and herbal/traditional medications e.g. St John's wort | See also Drug Interactions with DTG on page 8<br>If in any doubt, call the **HIV Hotline 0800 212 506** |
| RE-sistance | E | Consider HIV drug resistance if other causes of virological failure have been excluded and the client is adherent to their medication. | Refer to the algorithm "Management of virological failure on TLD" on page 18 |

## *Clinician considerations for providing Enhanced Adherence Counselling (EAC):*

| Barrier to adherence | Intervention | EAC indicated? |
|---|---|---|
| **Difficulty getting to facility to collect treatment** | Reduce unnecessary visits through enrolling client in a RPCs model or providing multi-month dispensing (MMD) | No need for EAC |
| **Drug side effects or unpalatability impacting adherence?** | Change to more palatable regimen | No need for EAC |
| **Challenges with taking/remembering to take treatment** | Provide EAC | |

## *Enhanced Adherance Support*

Enhanced Adherence Counselling (EAC) is aimed at non-stable clients presenting with adherence issues or poor treatment response and/or signs of treatment failure. Enhance Adherence Counselling focuses on:

- Providing education on the outcome of their latest clinical assessment and VL results
- Understanding what the client already knows or doesn't know regarding their treatment and the importance of VL suppression
- Doing a mental health screen
- Correcting any misconceptions and allowing flexibility around the most common barriers to adherence (such as alcohol/ drug consumption, forgetting doses due to a rigid schedule, etc.).
- Assessing and understanding the barriers that affect the client's adherence
- Developing adherence strategies to overcome these barriers.

To support the above processes, the following useful tools extracted from the Adherence Guideline SOPs are included in the annexures:

- SOP 2 Enhanced Adherence Counselling SOP (Annexure 3)
- Mental Health Screen (Annexure 4)
- Child and adolescent disclosure counseling for children living with HIV (Annexure 7)

## *Management of Virological Failure on TLD*

*(also applicable to other DTG-containing regimens)*

**Two** or more **VLs ≥ 1000** c/mL

On **TLD** for **at least 2 years**
and 2 elevated VLs were taken two or more years after starting TLD regimen

On TLD for **less than** 2 years, irrespective of VL

**Adherence > 80%**
Proven by an objective measurement [1]

**Adherence < 80%** [1]

**Repeat VL at next scheduled routine VL** (i.e., in 6 months' time)

Intensify efforts to **resolve adherence issues**[3] as outlined on page 17

**TLD 2**
Clients who have failed a previous ART regimen

**TLD 1**
Clients who have never failed a previous ART regimen

As a rule, resistance testing is **not indicated** for clients on **TLD1** [2]

**Special circumstances**[4]
e.g., incorrect classification as TLD1 (including perinatally infected adolescents), or drug interactions

**Additional considerations if VL > 1000 c/mL:**

- Monitor CD4 count every 6 months (See page 15).
- If CD4 < 200 cells/mm3, discuss with an HIV expert
- Consider eligibility for cotrimoxazole prophylaxis (see page 7)

**Discuss with an HIV expert** [5]
to authorise and interpret a resistance test*

**Individualised regimen**
as recommended by HIV expert [5]

**Repeat VL 3 months after starting the new regimen**
to confirm viral re-suppression

***Resistance testing** is expensive and should be done only for exceptional cases failing TLD1. Provinces should ensure that a gatekeeping function is in place by using either a designated provincial mechanism or the National TL committee to authorise resistance testing.

1. Objective measures of good adherence include at least one of:
   - Pharmacy refills > 80% in the last 6-12 months (if this is known)
   - Attendance of > 80% of scheduled clinic visits in the last 6-12 months (if this is known)
   - Detection of current antiretroviral drug/s in the client's blood or urine, if available

   Note: Self-reported adherence is not considered a measure of good adherence!
2. Due to their high genetic barrier, resistance to a first-line DTG-containing regimen (TLD1) is extremely rare. If other reasons for an unsuppressed VL have been addressed or excluded, e.g., drug interactions and the client remains unsuppressed at their repeat VL, suboptimal adherence remains the most probable cause for non-suppression. The highest probability of improving adherence would be to remain on a once-daily, well-tolerated, fixed-dose combination regimen (TLD) while identifying and addressing the underlying root causes of non-adherence. 99,9% of these clients will re-suppress on TLD if adherent!
3. Repeat the ABCDE assessment as outlined on page 17. Remember to ask about treatment side-effects, the potential cost of transport or loss of income related to clinic visits, mental health conditions, non-disclosure, poor social support, or substance abuse. If necessary, discuss with an expert or refer to other multidisciplinary team members, if available.
4. Special circumstances that may warrant a resistance test for clients on TLD1 include:
   - Incorrect classification as TLD1 (clients who declare themselves as never having had ART before, but who have actually been exposed to ART and may have failed a regimen in the past)
   - Perinatally infected adolescents: Unless a clearly documented drug history is available, perinatally infected adolescents should be classified as TLD2 due to the high likelihood of ART exposure and virological failure in the past
   - Current or previous drug interactions with rifampicin, carbamazepine, phenytoin, phenobarbital, or the polyvalent cations may have resulted in the development of resistance. Drug interactions may also warrant an expert discussion and authorisation of a resistance test earlier than 2 years on the regimen.

   In these types of exceptional circumstances, TLD1 clients with persistent virological failure despite confirmed good adherence may be discussed with an expert to authorise a resistance test on a case-by-case basis.
5. For advice from an HIV expert, approach an HIV Hotline, an infectious disease specialist, or the Third Line ART committee

If in doubt about any aspect of viral load management or switching to second-line, contact one of the following resources:

National HIV & TB Health Care Worker Hotline: **0800 212 506**
Right to Care Paediatric, Adolescent and Adult HIV Helpline: **082 352 6642**
KZN Paediatric Hotline: **0800 006 603**

ART, Antiretroviral therapy; DTG, Dolutegravir; LLV, Low-level viraemia; TL, Third-line; TLD, fixed-dose combination of tenofovir, lamivudine, DTG; VL, Viral load.

≥2.0 kg and ≥35 weeks gestational age at birth

Birth to <4 weeks of age

≥3.0 kg AND ≥4 weeks of age

**AZT + 3TC + NVP** → **ABC + 3TC + DTG**

### Baseline Assessment

- Clinical review
- Bloods: confirmatory HIV PCR, CD4 count, FBC +/- HIV drug resistance test if mother failing treatment on protease inhibitor / dolutegravir regimen
- Counsel parent / caregiver
- Ensure mother on ART / advise on breastfeeding

### Review after 1 week then 1-2 weekly

- Clinical review and counselling
- Check baseline blood results
- If indeterminate / negative confirmatory HIV PCR test result, refer to Guideline for Family-Centered Transmission Prevention of Communicable Infections

### Review when 4 weeks of age

- Clinical review and counselling
- If <3 kg, assess reasons for poor weight gain & manage appropriately, continue ART with AZT (12 mg/kg/dose twice daily) + 3TC (4 mg/kg/dose twice daily) + NVP (6 mg/kg/dose twice daily) until ≥3.0 kg
- If >3 kg, switch ART to ABC + 3TC + DTG (refer to ARV dosing chart for doses)
- Continue monitoring and evaluations as per section 9.1.3

| | Lamivudine (3TC) | | Zidovudine (AZT) | | Nevirapine (NVP) | |
|---|---|---|---|---|---|---|
| Available formulation | Solution 10 mg/mL | | Solution 10 mg/mL | | Solution 10 mg/mL | |
| Weight (kg) at birth | Dose | | Dose | | Dose | |
| | **AM** | **PM** | AM | PM | AM | PM |
| ≥2.0 – <3.0 | 5 mg (0.5 mL) | 5 mg (0.5 mL) | 10 mg (1 mL) | 10 mg (1 mL) | 15 mg (1.5 mL) | 15 mg (1.5 mL) |
| ≥3.0 – <4.0 | 8 mg (0.8 mL) | 8 mg (0.8 mL) | 15 mg (1.5 mL) | 15 mg (1.5 mL) | 20 mg (2 mL) | 20 mg (2 mL) |
| ≥4.0 – <5.0 | 10 mg (1 mL) | 10 mg (1 mL) | 20 mg (2 mL) | 20 mg (2 mL) | 30 mg (3 mL) | 30 mg (3 mL) |

<2.0 kg
OR
<35 weeks
gestational age
at birth

Birth to < 4 weeks of age
OR < 3 kg

≥ 4 weeks of age
AND
≥ 3 kg

**AZT + 3TC + NVP** → **ABC + 3TC + DTG**

### Baseline Assessment
- Clinical review
- Bloods: confirmatory HIV PCR, CD4 count, FBC +/- HIV drug resistance test if mother failing treatment on protease inhibitor or dolutegravir regimen
- Counsel parent / caregiver
- Ensure mother on ART / advise on breastfeeding

### Review after 1 week then 1-2 weekly
- Clinical review and counselling
- Check baseline blood results
- If indeterminate / negative confirmatory HIV PCR test result, refer to Guideline for Family-Centered Transmission Prevention of Communicable Infections
- Monitor weight gain and adjust ARV doses

### Review when ≥4 weeks of age
- Clinical review and counselling
- If <3 kg, continue AZT + 3TC + NVP
- If >3 kg, switch to ABC + 3TC + DTG (refer to ARV dosing chart for doses)
- Continue monitoring and evaluations

| Gestational age at birth | Chronological age | Zidovudine (AZT) | Lamivudine (3TC) | Nevirapine (NVP) |
|---|---|---|---|---|
| | | Solution 10 mg/mL | Solution 10 mg/mL | Solution 10 mg/mL |
| <30 weeks | Birth - <4 weeks | 2 mg/kg/dose twice daily | 2 mg/kg/dose twice daily | 2 mg/kg/dose twice daily |
| | >4 weeks - <8 weeks | 3 mg/kg/dose twice daily | 4 mg/kg/dose twice daily | 4 mg/kg/dose twice daily |
| | >8 weeks - <10 weeks | 12 mg/kg/dose twice daily | | 6 mg/kg/dose twice daily |
| | Birth - <2 weeks | 2 mg/kg/dose twice daily | 2 mg/kg/dose twice daily | 2 mg/kg/dose twice daily |
| ≥30-<35 weeks | >2 - <4 weeks | 3 mg/kg/dose twice daily | | 4 mg/kg/dose twice daily |
| | >4 - <6 weeks | | 4 mg/kg/dose twice daily | 6 mg/kg/dose twice daily |
| | >6 - <8 weeks | 12 mg/kg/dose twice daily | | |

*When weight is ≥2 kg and ≥35 weeks corrected gestational age, review ARVs and refer to Table xx*

# Annexure 3 *Enhanced Adherence Counselling*

*Source: National Adherence Guideline 2023*

## ENHANCED ADHERENCE COUNSELLING SESSIONS

There are two sessions:
Session 1: Initial enhanced adherence counselling for patients struggling with adherence.
Session 2: Enhanced adherence counselling for persistent non-adherent patients (covered in Adherence Guideline SOP2).

## SESSION 1

### 1. Explain the purpose of your session, define terms:

- Determine possible reasons for abnormal assessment results.
- Assess and address any reported barriers to adherence and discuss effective strategies to overcome.
- Update or develop an adherence plan with the patient.

### 2. Education on the assessment result

- Assess patient for mental health using the Mental Health Assessment tool in Annexure II.
- Find out what treatment education the patient has received.
- Find out what the patient knows about the treatment they are taking and check the treatment regimen has been understood correctly i.e. when each medicine is taken.
- Explain in a supportive way that the most common reason for such result is a problem with taking medication correctly.
- Find out if the patient received education on the assessment to check adherence and effective treatment( VL/BP/HbA1c) and its meaning. If not, provide this information (see SOP 1: FTIC session 2).

### 3. Flexibility on treatment

- Clear any myths and misconceptions around taking treatment and explain that there is some flexibility.
- Emphasize the importance of patients choosing their own suitable time for taking medication as prescribed.
- Explain what to do with late or missed doses depending on the treatment.
- Explain what to do in case of alcohol use while on treatment. If patient cannot control their use of alcohol, they should make sure that they take their treatment anyway.
- Explain to patient that it is better not to use traditional medicines that could interfere with the treatment. If they take traditional medicine, they should make a plan with the clinician to still take their treatment.

### 4. Patient's experiences

Ask: What makes it difficult for you to take the treatment sometimes? Encourage the patient to be honest about personal issues that may affect their adherence and help them to address issues such as alcohol or other substance intake as they can lead to forgetting medication.

- Explain that medication should be taken even without food and what they can do if food insecurity is an issue. Inform and assist patient on how to access government support programmes, if necessary.
- Consider patient's religious and traditional beliefs that may contribute to non-adherence to treatment.

### 5. Identify strategies to ensure good adherence

Ask: What could help you to remember to take the treatment?

Discuss treatment reminders and adherence options including the advantages and disadvantages of each for the specific patient:

- Treatment buddy to remind the patient to take treatment
- Setting phone alarm
- Support by a family member
- Pill counts
- Marking a calendar or using a pill box
- Linking medication to meal times
- Modified Direct Observed Therapy such as treatment supporter (this is also applicable to children)

Ask: Who could support you to take the treatment every day?

Discuss sources of social support for the client. Emphasise the importance of support structures in coping and adherence such as family, friends, peer support groups, faith-based group and work-based support.

- Encourage sharing of feelings and emotions regarding the illness.
- Empower the patient in making a plan that is adapted to the barriers expressed. Be aware not to create dependency, but to find their own solutions, with the help of the healthcare worker or lay counsellor.

### 6. Inform the patient about pathway ahead

- Explain further assessments (tests) to check adherence and effective treatment as per disease specific guidelines (for HIV: a further viral load will be taken in 3 months, for hypertension: a BP will be taken at every visit for the next 3 months, for diabetes: a further HbA1c test will be done in 3 months)
- Explain that if the next assessment is normal, it will become easier to collect treatment. The patient can ask and the clinician should offer and enroll the patient into a simpler treatment supply collection system of their choice with longer treatment supply based on what is available at the facility (FAC-PUP/Adherence Club/EX-PUP).

## Annexure 4 *Mental Health Assessment*

*Source: National Adherence Guideline 2023*

As mental health disorders can impact adherence negatively, it is recommended that screening is provided for mental health disorders while treating HIV, TB and NCDs.

Basic screening should assess:

### 1. What is the patient's appearance?

- Is he/she clean and looking after him or herself
- Does the person look worried or sad?
- Does the person seem agitated?
- Does he/she seem suspicious, nervous or hostile?

### 2. Assess the patient's mood, asking:

- How have you been feeling over the last week?
- Have you been feeling mostly normal, or sad or happy, or worried?
- How do you feel today?
- What are your feelings about the future?

### 3. Assess the patient's thoughts:

- Are you having negative thoughts?
- Are you having strange thoughts?
- Any unusual fears (such as being followed, spied on)?
- Have you had any strange experiences (such as hearing voices/seeing visions other people cannot hear or see) or special abilities?

Negative thoughts can suggest depression, other strange thoughts or experiences could raise suspicion of psychosis.

### 4. Assess patient's cognition:

- Does thinking seem slow?
- Is the person able to concentrate?
- Does the memory seem impaired?

If you suspect a mental health disorder while asking the previous questions, try to answer the following questions:

- What is the main problem?
- How long has it been present?
- Does it affect the patient's daily functioning?
- Can this be managed at this clinic?

If further assessment and treatment cannot be provided at the clinic, refer to a psychiatric nurse or service. Tools such as SRQ 20 recommended by the WHO can help to identify mental health disorder.

Provide the patient with education on mental health and provide them with advice that can help them overcome symptoms. Explain to the patient that the following signs could mean that they may need support to improve their mental health condition:

If they feel:

- constantly angry or very worried
- very sad for a very long time
- they are losing interest in things they use to enjoy doing
- they can not cope with work or daily activities
- their mind is controlled (such as by voices) or out of control
- they need to use alcohol or drugs
- Obsessively do things such as repeat washing hands, non-stop sport activity, eating too much, obsessive diet or other obsessive behaviours.
- Hurt themselves or other people or destroy things.
- Do irresponsible things that could harm them or others.
- Having problems sleeping or feeling tired and not having energy.
- Feeling anxious, looking or feeling 'jumpy' or upset, having panic attacks.
- Not wanting to spend time with people; spending too much time in bed.
- Hearing and seeing things that others do not see.

Other differences in the way the person sees what is happening around them, for example believing that someone is trying to harm you, or laughing at you.

> ! If the patients show signs of intense sadness, risk to harm themselves or others or hear or see things that other do not see they should directly be referred for psychiatric support.

If the patients experience some of the other symptoms, explain to them that they can identify some ways to help them cope with their situation by telling them that it might help to:

- Share your feelings and spend time with other people you trust.
- Get back to daily routine as much as possible (such as work, school, housework).
- Participate in religious or spiritual activities.
- Play sports or get regular exercise.
- Eat regular meals.
- Get adequate rest.
- Take a break and relax.
- Participate in enjoyable activities (such as singing, dancing, reading), even if at the moment it may be hard for you to enjoy them.
- Help other people talk about how they feel, but also respect if they choose not to talk about it.

Recommend that they avoid:

- Using alcohol or drugs to cope with the symptoms
- Withdrawing from family and friends
- Withdrawing from daily activities
- Overworking
- Blaming yourself or others
- Neglecting your health or self-care (such as sleep, hygiene, diet)

Explain that the patient, may need to seek help from a psychiatric nurse, social worker, psychologist or counsellor if they want to talk with someone outside of their family or circle of friends or if their symptoms do not improve with coping strategies.

# Annexure 5 *Antiretroviral Drug Dosing Chart for Children (2022)*

Compiled by Child and Adolescent Committee of SA HIV Clinicians Society in collaboration with the Department of Health

| | **Abacavir + Lamivudine (ABC + 3TC)** | **Dolutegravir (DTG)** | **Dolutegravir when on Rifampicin** | **Abacavir (ABC)** | **Lamivudine (3TC)** | **Zidovudine (AZT)** |
|---|---|---|---|---|---|---|
| **Target dose** | As for individual medicines **ONCE daily** | By weight band **ONCE daily** | By weight band **TWICE DAILY** | 8 mg/kg/dose **TWICE daily** OR **If ≥ 10 kg:** 16 mg/kg/dose **ONCE daily** | 4 mg/kg/dose **TWICE daily** OR **If ≥ 10 kg:** 8 mg/kg/dose **ONCE daily** | 180 - 240 mg/m$^2$/dose **TWICE daily** |
| **Available formulations** | Dispersible tablet FDC: ABC/3TC 120/60 mg Tablets FDC: ABC/3TC 600/300 mg ABC/3TC/DTG 600/300/50 mg | Dispersible tabs (DT) 10 mg, Film coated (FC) tabs 50 mg, FDC: TLD 300/300/50 mg OR ABC/3TC/DTG 600/300/50 mg **DT AND FC TABLETS ARE NOT BIOEQUIVALENT** | Dispersible tabs (DT) 10 mg, Film coated (FC) tabs 50 mg, FDC: TLD 300/300/50 mg OR ABC/3TC/DTG 600/300/50 mg **DT AND FC TABLETS ARE NOT BIOEQUIVALENT** | Sol. 20 mg/ml Tabs 60 mg (scored, dispersible), 300 mg (not scored) | Sol. 10 mg/ml Tabs 150 mg (scored) | Sol. 10 mg/ml Tabs 100 mg, 300 mg (not scored), FDC: AZT/3TC 300/150 mg |
| **Wt. (kg)** | Consult with a clinician experienced in paediatric ARV prescribing for neonates (< 28 days of age) and infants weighing < 3kg | | | | | |
| **3 - 5.9** | 1 x 120/60 mg tab od | 0.5 x 10 mg DT od | 0.5 x 10 mg DT bd | 3 ml bd **OR** 1 x 60 mg tab bd | 3 ml bd | 6 ml bd |
| **6 - 9.9** | 1.5 x 120/60 mg tabs od | 1.5 x 10 mg DT od | 1.5 x 10 mg DT bd | 4 ml bd **OR** 1.5 x 60 mg tab bd | 4 ml bd | 9 ml bd |
| **10 - 13.9** | 2 x 120/60 mg tabs od | 2 x 10 mg DT od | 2 x 10 mg DT bd | Once daily dosing > 10 kg<br>4 x 60 mg tabs od **OR** 12 ml od | Once daily dosing > 10 kg<br>12 ml od | 12 ml bd **OR** 1 x 100 mg tabs bd |
| **14 - 19.9** | 2.5 x 120/60 mg tabs od | 2.5 x 10 mg DT od | 2.5 x 10 mg DT bd | 5 x 60 mg tabs od **OR** 1 x 300 mg tab od | 1 x 150 mg tab od | 2 x 100 mg tabs am + 1 x 100 mg tab pm **OR** 15 ml bd |
| **20 - 24.9** | 3 x 120/60 mg tabs od | 3 x 10 mg DT od **OR** 1 x 50 mg FC tab od | 3 x 10 mg DT bd **OR** 1 x 50 mg FC tab bd | 1 x 300 mg tab + 1 x 60 mg tab od **OR** 6 x 60 mg tabs od | 2 x 150 mg tabs od | 2 x 100 mg tabs bd **OR** 20 ml bd |
| **25 - 29.9** | 1 x 600/300 mg tab od **OR** ABC/3TC/DTG FDC (600/300/50 mg) if eligible od | 1 x 50 mg FC tab od **OR** FDC: ABC/3TC/DTG if eligible od | 1 x 50 mg FC tab bd OR FDC: ABC/3TC/ DTG if eligible od + 50 mg DTG FC tab 12 hours later | 2 x 300 mg tabs od | | 1 x 300 mg tab bd **OR** 1 x AZT/3TC 300/150 mg tab bd |
| **30 - 39.9** | | 1 x 50 mg FC tab od **OR** FDC: TLD if eligible od **OR** FDC: ABC/3TC/DTG if eligible od | 1 x 50 mg FC tab bd **OR** FDC: TLD if eligible od + 50 mg DTG FC tab 12 hours later **OR** FDC: ABC/3TC/ DTG if eligible od + 50 mg DTG FC tab 12 hours later | | | |
| **≥ 40** | | | | | | |

* Avoid LPV/r solution in any full-term infant <14 days of age and any premature infant <42 weeks post conceptual age (corrected gestational age) or obtain expert advice.

✦ Children weighing 25-29.9 kg may also be dosed with LPV/r 200/50 mg adult tabs: 2 tabs am + 1 tab pm.

# Atazanavir + ritonavir should not be used in children/adolescents on treatment with Rifampicin, obtain expert advice. No dosage adjustments are required for children receiving treatment with Efavirenz and Rifampicin.

od = once a day;
nocte = at night;
bd = twice a day;
am = in the morning;
pm = in the evening;

| Lopinavir / ritonavir (LPV/r) | Abacavir + Lamivudine + Lopinavir/ ritonavir | Lopinavir/ritonavir when on rifampicin (and for 2 weeks after stopping rifampicin) | | # Atazanavir (ATV) + Ritonavir (RTV) | Efavirenz (EFV) | |
|---|---|---|---|---|---|---|
| 300/75 mg/m²/dose LPV/r **TWICE daily** | **By weight band TWICE daily** | LPV/r std dose + super-boosting with ritonavir (RTV) powder **TWICE daily** (≥ 0,75 x LPV dose bd) | Double-dose LPV/r tabs ONLY if able to swallow whole LPV/r tabs **TWICE daily** | By weight band **ONCE daily** | By weight band **ONCE daily** | **Target dose** |
| Sol. 80/20 mg/ml<br>Adult tabs 200/50 mg,<br>Paed tabs 100/25 mg<br>**TABLETS MUST BE SWALLOWED WHOLE**<br>Pellets 40/10 mg per capsule<br>**ONLY FOR USE IF NOT TOLERATING LPV/r SOLUTION. CAPSULES ARE NOT RECOMMENDED < 6 MONTHS OF AGE** | Caps 30/15/40/10 mg<br>**IF PATIENT IS ON RIFAMPICIN TB TREATMENT, ADD RTV POWDER** (next column) | Oral powder 100 mg/packet | Adult tabs 200/50 mg, **Paed tabs** 100/25 mg | ATV caps 150, 200 mg; RTV tabs 100 mg; FDC: ATV/RTV 300/100 mg RTV TABLETS AND ATV/r FDC TABLETS MUST BE SWALLOWED WHOLE | Caps/tabs 50, 200, 600 mg; FDC: TEE 300/200/600 mg; TABLETS MUST BE SWALLOWED WHOLE | **Available formulations** |
| Consult with a clinician experienced in paediatric ARV prescribing for neonates (< 28 days of age) and infants weighing < 3kg | | | | | | **Wt. (kg)** |
| * 1 ml bd<br>**OR**<br>2 capsules bd | 2 capsules bd | LPV/r std dose (see purple column) + oral RTV powder 100 mg (1 packet) bd | Do not use double-dose LPV/r tabs | Not recommended | Not recommended | **3 - 5.9** |
| * 1.5 ml bd<br>**OR**<br>3 capsules bd | 3 capsules bd | | | | | **6 - 9.9** |
| 2 ml bd OR 4 capsules bd<br>**OR**<br>2 x 100/25 mg paed tabs am + 1 x 100/25 mg paed tab pm | 4 capsules bd | LPV/r std dose (see purple column) + oral RTV powder 200 mg (2 packets) bd | 3 x 100/25 mg **paed tabs** bd | ATV 1 x 200 mg cap od + RTV 1 x 100 mg tab or 100 mg oral powder (1 packet) od | 1 x 200 mg cap/tab nocte | **10 - 13.9** |
| 2.5 ml bd OR 5 capsules bd<br>**OR**<br>2 x 100/25 mg paed tabs bd<br>**OR**<br>1 x 200/50 mg adult tab bd | 5 capsules bd | | 4 x 100/25 mg **paed tabs** bd<br>**OR**<br>2 x 200/50 mg **adult tabs** bd | | 1 x 200 mg cap/tab + 2 x 50 mg caps/ tabs nocte | **14 - 19.9** |
| 3 ml bd OR 6 capsules bd OR 2 x 100/25 mg paed tabs bd OR 1 x 200/50 mg adult tab bd | 6 capsules bd | | | | | **20 - 24.9** |
| 3.5 ml bd OR 7 capsules bd OR 3 x 100/25 mg paed tabs bd OR 1 x 200/50 mg adult tab bd + 1 x 100/25 mg paed tab bd | Not recommended | LPV/r std dose (see purple column) + oral RTV powder 300 mg (3 packets) bd | 6 x 100/25 mg **paed tabs** bd<br>**OR**<br>3 x 200/50 mg **adult tabs** bd | 1 x ATV/RTV 300/100mg FDC od<br>**OR**<br>ATV 2 x 150 mg caps od + RTV 1 x 100 mg tab or 100 mg oral powder (1 packet) od | 2 x 200 mg caps/ tabs nocte | **25 - 29.9** |
| 5 ml bd OR 10 capsules bd<br>**OR**<br>4x100/25 mg paed tabs bd<br>**OR**<br>2x200/50 mg adult tabs b | | | 8 x 100/25 mg **paed tabs** bd<br>**OR**<br>4 x 200/50 mg **adult tabs** bd | | | **30 - 39.9** |
| | | | | | 2 x 200 mg caps/ tabs nocte **OR** FDC: TEE if eligible od | **≥ 40** |

std = standard;
FDC = fixed dose combination;
TLD = tenofovir/lamivudine/dolutegravir;
TEE = tenofovir/emtricitabine/efavir

| Weight (kg) | 3 - 5.9 | 6 - 13.9 | 14 - 24.9 | ≥ 25 |
|---|---|---|---|---|
| **Cotrimoxazole Dose** | 2.5 ml od | 5 ml or ½ tab od | 10 ml or 1 tab od | 2 tabs od |
| **Multivitamin Dose** | 2.5 ml od | 2.5 ml od | 5 ml od | 10 ml od |

| ARV Drug | Formulations (as used in dosing chart) | Can tablets/capsules be split/crushed/ opened if unable to swallow? | Comment |
|---|---|---|---|
| **Abacavir (ABC)** | Oral solution: 20 mg/ml<br>Tablets: 60 mg, 300 mg<br>FDC tablets: ABC/3TC 120/60 mg;<br>ABC/3TC 600/300 mg;<br>ABC/3TC/DTG 600/300/50 mg<br>FDC capsules: ABC/3TC/LPV/r 30/15/40/10 mg | Tablets: **YES**<br><br>FDC 120/60 mg tablet is a dispersible tablet. May be split/crushed.<br>FDC capsules should be opened and contents added to a small amount of food or dispersed in a liquid. | Hypersensitivity reaction (fever, rash, GIT & respiratory symptoms) may occur during first 6 weeks of therapy, very uncommon in black African patients. Symptoms typically worsen in the hours immediately after the dose and after each subsequent dose. Caregivers or patients should discuss symptoms early with the clinician rather than stopping therapy. Stop ABC permanently if hypersensitivity reaction has occurred. |
| **Lamivudine (3TC)** | Oral solution: 10 mg/ml<br>Tablets: 150 mg; FDC tablets: ABC/3TC 120/60 mg; ABC/3TC 600/300 mg, TLD 300/300/50 mg<br>ABC/3TC/DTG 600/300/50 mg FDC capsules:<br>ABC/3TC/LPV/r 30/15/40/10 mg | | Well tolerated, adverse-effects uncommon. Pure red cell aplasia causing anaemia can occur but is very rare. |
| **Zidovudine (AZT)** | Oral solution: 10 mg/ml<br>Tablets: 100 mg, 300 mg<br>Capsules: 100 mg<br>FDC tablet: AZT/3TC 300/150 mg | Tablets and FDC: **YES**<br>Capsules: Can be opened and added to a small amount of soft food/liquid and ingest immediately. | Avoid or use with caution in neonates or children with anaemia (Hb <8 g/dl) due to potential to cause bone marrow suppression. |
| **Tenofovir (TDF)** | Tablets: 300 mg<br>FDC tablets: TDF/FTC 300/200 mg,<br>TEE 300/200/600 mg, TLD 300/300/50 mg | Tablet and FDC tablets: **YES** | TDF may be prescribed for adolescents ≥ 10 years of age AND ≥ 30 kg body weight after ensuring adequate renal function by checking eGFR/creatinine using the appropriate formula (refer to HIV guidelines). TDF is usually prescribed as part of an FDC tablet: TDF/FTC, TDF/FTC/EFV or TDF/3TC/DTG. To assess for TDF-induced nephrotoxicity, do creatinine and eGFR at months 3, 6 and 12 and thereafter repeat every 12 months. |
| **Lopinavir/ ritonavir (LPV/r)** | Oral solution: 80/20 mg/ml<br>Capsules: Pellets 40/10 mg per capsule<br>Tablets: 200/50 mg, 100/25 mg<br>FDC capsules: ABC/3TC/LPV/r 30/15/40/10 mg | Tablets: **NO**<br>**Must be swallowed whole and not divided, crushed or chewed.**<br>Capsules: Can be opened and added to a small amount of soft food/liquid and ingest immediately. | Oral solution should be refrigerated/stored at room temperature (if <25°C) for up to 6 weeks. Preferably administer oral solution with food as increases absorption. Strategies to improve tolerance and palatability of oral solution: coat mouth with peanut butter, dull taste buds with ice, follow dose with sweet foods. Many drug-drug interactions.#<br>LPV/r 40/10 mg capsules should be opened, and contents (pellets) of each capsule poured onto a spoon of soft food and fed to child. Don't try and dissolve pellets in food or water as they will develop a bad taste. ABC/3TC/LPV/r capsules should be opened and contents (granules) of each capsule poured onto a spoon of soft food or dissolved in water and fed to child. Capsules should never be swallowed whole. Discard capsule casing after contents have been emptied from it. |
| **Ritonavir (RTV)** | Oral powder: 100 mg/packet<br>Tablets: 100 mg | | Each 100 mg packet of RTV powder should be mixed with a small amount of water or soft food and immediately ingested. Many drug-drug interactions.# |
| **Atazanavir (ATV)** | Capsules: 150 mg, 200 mg<br>FDC tablets: ATV/RTV 300/100 mg | Capsules: Can be opened and added to a small amount of soft/food/liquid and ingested immediately.<br>FDC tablets: **NO**<br>**Must be swallowed whole and not divided, crushed or chewed.** | ATV is used in combination with RTV. May cause unconjugated hyperbilirubinaemia resulting in jaundice but this does not indicate hepatic toxicity and not a reason to discontinue the drug unless it is worrying the patient. Consider drug-drug interactions.# |
| **Dolutegravir (DTG)** | Dispersible tablet (DT): 10 mg<br>Film coated (FC) tablets: 50 mg<br>FDC tablets: TLD 300/300/50 mg<br>FDC tablets: ABC/3TC/DTG 600/300/50 mg | Dispersible tablets: **YES**<br>Film coated tablets (including FDCs): **YES** | Iron supplements decrease DTG concentrations if taken together on an empty stomach. To prevent this, DTG and iron supplements can be taken at the same time if taken with food. May be helpful to administer as a morning dose rather than an evening dose if insomnia occurs with evening dosing. May raise creatinine levels by up to 15% without affecting renal function. Consider drug-drug interactions. #<br>DTG DT and DTG FC tablets are not bioequivalent; 30 mg of DTG DT corresponds to 50 mg DTG FC tablets. DTG 50 mg FC tablets are preferred for children who have reached 20 kg (unless they cannot swallow tablets). |
| **Efavirenz (EFV)** | Capsules: 50 mg, 200 mg<br>Tablets: 50 mg, 200 mg, 600 mg<br>FDC tablets: TEE 300/200/600 mg | Tablets: **NO**<br>**Must be swallowed whole and not divided, crushed or chewed.**<br>Capsules: **YES**. Open and add to small amount of soft food and ingest immediately | Best given at bedtime to reduce CNS side-effects, especially during first 2 weeks. Consider drug-drug interactions.# |

#EML-Antiretroviral interactions table (http://www.mic.uct.ac.za)
OR www.hiv-druginteractions.org/checker
OR the Liverpool HIV iChart application for smart phones, or any of the helplines:
National HIV and TB Health Care Worker Hotline: 0800 212 506
OR Right to Care Paediatric, Adolescent and adult HIV Helpline: 082 352 6642
and KZN Paediatric Hotline: 0800 006 603

FDC = fixed dose combination;
eGFR = estimated glomerular filtration rate;
GIT = gastrointestinal tract;
TEE = Tenofovir/Emtricitabine/Efavirenz;
TLD = Tenofovir/Lamivudine/Dolutegravir;

# STEP BY STEP GUIDE TO DISCLOSURE TO CHILDREN REGARDING THEIR HIV STATUS

- Remains a difficult process for all concerned
- Effective conversations are dependent on the age and understanding (developmental level) of the child
- Aim to build up a body of knowledge in the child that leads to the point of disclosure of HIV diagnosis
- The first step is to find out what the child already knows (often more than adults think)

Failure of full disclosure by early teenage years can lead to:

- Poor adherence
- Emotional difficulties
- Poor school performance
- HIV transmission if sexually active

## VERY YOUNG

0 – 4 Years
NO DISCLOSURE YET

### DEVELOPMENTAL LEVEL

- Depends on adult for all needs and information
- Child needs comfort, support and most of all security

### WHAT DO YOU EXPLAIN:

- Carry on consultation with child present
- Child too young for direct information about HIV but explanations to caregiver about how HIV can affect the child remain important
- Provide ideas to help caregiver support child taking medicine
- Congratulate child on taking medicines well
- Address caregiver anxieties
- Build relationship with the child through play/singing
- Provide a safe and welcoming clinic

### AIM

BUILD UP CONFIDENCE of CHILD in HEALTH WORKERS and MEDICINE TAKING

## YOUNG CHILD

(PRE-SCHOOL)
5 – 7 Years
EARLY DISCLOSURE

### DEVELOPMENTAL LEVEL

- Can understand concrete based ideas e.g. real events in the present and past
- Thinking is based in the present
- Take the lead from confidence of caregiver interactions with health workers
- Beginning to link medicines and health

### WHAT DO YOU EXPLAIN:

Child needs to learn about illness but not HIV by name yet

- Introduce ideas of good and bad health by eating healthy food, keeping clean, exercising, looking after teeth etc.
- Medicines help to keep a body healthy and strong
- Introduce infections as 'germs' that can hurt or damage the body/make you sick or hurt
- Introduce (white) blood cells as the part of the body that look for and kill infections or germs
- Some germs hide and you need to take medicines to help fight the germs

### AIM

UNDERSTANDING that MEDICINES SUPPORT the BODY to KEEP YOU WELL

## SCHOOL GOING CHILD

8 – 10 YRS
PARTIAL DISCLOSURE

### DEVELOPMENTAL LEVEL:

- Able to hold onto ideas and apply them to new situations
- Can understand past, present and future
- Has social and moral awareness about right & wrong behaviour
- Beginning to be more curious and take some control over their lives

### WHAT DO YOU EXPLAIN:

- Explain that the germ concerned is a virus
- Viruses are 'clever germs' which can damage white blood cells
- If medicines are not taken correctly, the virus can get stronger and stop the medicines from working (resistance)
- Naming of the virus as HIV may occur but is not essential
- Need to explain that information is private and should only be shared with those agreed with the caregiver(s)
- Help the child identify who they can talk to about their health or HIV
- Disclosure to symptomatic school age children is strongly encouraged

### AIM

NAMING of INFECTION as HIV VIRUS

## TEENAGER

11 – 19 Years
FULL DISCLOSURE

### DEVELOPMENTAL LEVEL:

- More abstract thinking (understands future consequences of actions)
- Increasingly making decisions on their own regarding identity, independence, school, career
- Puberty/sexual development
- Dependence on caregivers decreases
- Importance of relationships with friends increases

### WHAT DO YOU EXPLAIN:

- Check understanding of health, medicines, sexual development and HIV infection
- Directly address young person during clinic consultations
- Need to understand responsibility for not transmitting HIV i.e. safer sex, and their rights i.e. family planning, confidentiality
- Preparation for future, encourage direct involvement in discussions and decisions
- Promote the benefits of attendance at adolescent support group

### AIM

FULL UNDERSTANDING of RIGHTS and RESPONSIBILITIES
ABILITY to NEGOTIATE own HEALTH CARE

# Other Resources and Important Information

## *Adverse Drug Reactions*

Surveillance of all adverse drug reactions (ADRs) is fundamental. Active surveillance, especially amongst pregnant women choosing to take DTG, has become imperative. Healthcare professionals and consumers in South Africa are urged to report any ADRs to the National Adverse Drug Event Monitoring Centre at (021) 447 1618, or SAHPRA pharmacovigilance office at (012) 395 9133/8197/8155 or NDoH Pharmacovigilance Centre for Public Health Programmes at npc@health.gov.za / (012) 395 9506 using the ADR reporting form.

## *Drug Stock-outs*

To report drug stock-outs, or for assistance with drug stock-outs, please contact Stop Stockouts:
SMS/please call me/WhatsApp (084) 855-7867
Email: reports@stockouts.org

## *Resources for Clinical Management and Drug Interactions*

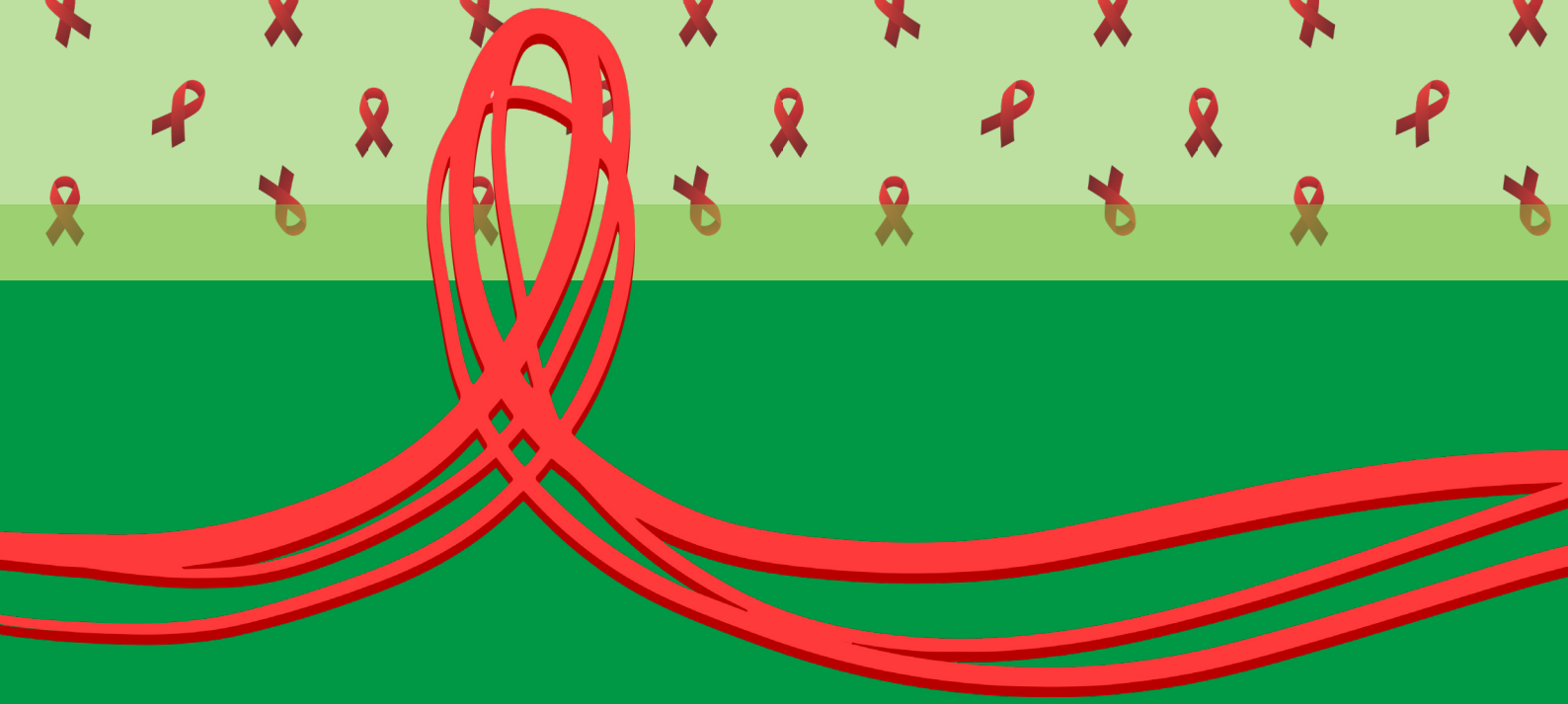
**National HIV & TB Health Care Worker Hotline:** 0800 212506
Email pha-mic@uct.ac.za
SMS/please call me/WhatsApp (071) 840-1572

**Right to Care Paediatric, Adolescent and Adult HIV Helpline (082) 352-6642**
**Both Right to Care Helplines can be contacted via call/ SMS/please call me/WhatsApp**

**KZN Paediatric Hotline:** 0800 006 603

## Abbreviations

| | |
|---|---|
| 3TC | Lamivudine |
| ABC | Abacavir |
| AGL | Adherence Guideline |
| ALT | Alanine transaminase |
| ANC | Antenatal Care |
| APC | Adult Primary Care |
| ART | Antiretroviral therapy |
| ARV | Antiretroviral |
| ATV/r | Atazanavir/ritonavir |
| AZT | Zidovudine |
| bd | Twice daily |
| BMI | Body mass index |
| CCMDD | Central Chronic Medicines Dispensing and Distribution |
| CM | Cryptococcal meningitis |
| CNS | Central nervous system |
| CPT | Cotrimoxazole preventive therapy |
| CrAg | Cryptococcal Antigen |
| CVS | Cardiovascular |
| DILI | Drug-induced liver injury |
| DR | Drug-resistant |
| DS | Drug-sensitive |
| DT | Dispersible tablet |
| DTG | Dolutegravir |
| eGFR | Estimated glomerular filtration rate |
| EFV | Efavirenz |
| FC | Film coated |
| FDC | Fixed-dose combination |
| Hb | Haemoglobin |
| HBsAg | Hepatitis B surface antigen |
| HBV | Hepatitis B virus |
| InSTI | Integrase strand transfer inhibitor |
| IRIS | Immune reconstitution inflammatory syndrome |
| IUCD | Intrauterine contraceptive device |
| LPV/r | Lopinavir/ritonavir |
| MTCT | Mother-to-child transmission |
| MUAC | Mid-upper arm circumference |
| NA | Not applicable |
| NCDs | Non-communicable diseases |
| NNRTI | Non-nucleoside reverse transcriptase inhibitor |
| NRTI | Nucleoside reverse transcriptase inhibitor |
| NTDs | Neural tube defects |
| NVP | Nevirapine |
| od | Once daily |
| OI | Opportunistic infection |
| PCR | Polymerase chain reaction test for HIV |
| PHC EML | Primary Health Care Essential Medicines List |
| PI | Protease inhibitor |
| PLHIV | People living with HIV |
| RT | Resistance test |
| sCR | Serum creatinine |
| STIs | Sexually transmitted infections |
| TB | Tuberculosis |
| TDF | Tenofovir disoproxil fumarate |
| TEE | Tenofovir + emtricitabine + efavirenz |
| TLD | Tenofovir + lamivudine + dolutegravir |
| TLE | Tenofovir + lamivudine + efavirenz |
| TPT | TB preventive treatment |
| VL | Viral load |
| WHO | World Health Organisation |
| WOCP | Women of childbearing potential |



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