2023 ART Clinical Guidelines

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

June 2023 Version 4

Republic of South Africa National Department of Health

S Afr Pharm J 2023;90(6):35-50

Foreword

South Africa is committed to attaining the UNAIDS 95-95-95 targets to control the HIV epidemic by providing quality healthcare services using highly effective antiretroviral treatment (ART). The principal goal of ART is to attain and maintain viral suppression, which will prevent new HIV infections, increase life expectancy, decrease morbidity and mortality as well as improve the quality of lives of all South Africans, thus contributing to realising the vision of A LONG AND HEALTHY LIFE FOR ALL.

The "Test and Treat All" approach has allowed people living with HIV (PLHIV) to access ART timeously.

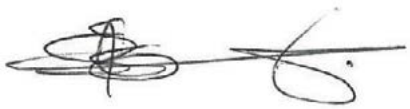
South Africa is committed to using available technology and evidence to continue the fight against HIV. The 2019 guidelines have been revised to include more optimised treatment regimens for all clients, including pregnant and breastfeeding women and children. The National Health Council (NHC) has adopted the new World Health Organization (WHO) recommended first, second and third-line regimens that include Dolutegravir (DTG) as the preferred antiretroviral drug.

I am introducing the 2023 ART guideline, which introduces simplified ART provision and harmonised methods of management of children, adolescents and adults, as well as pregnant women living with HIV/AIDS, TB and other common opportunistic infections. The guidelines also provide guidance on the use of Dolutegravir (DTG) dispersible tablets for children from 3 kg and 4 weeks old.

These guidelines have been revised with the Differentiated Models of Care SOPs to ensure simultaneous consideration and alignment of clinical, adherence and service delivery updates. The Differentiated Models of Care SOPs form part of this guidance to enable optimal use of decentralised and integrated service delivery to promote a patient-centred approach. Effective 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 urge all clinicians at PHC clinics, community health centres and hospitals across the board to use these guidelines diligently to offer quality, comprehensive services to the public.

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



Dr SSS Buthelezi
Director-General: Health
Date: 24-04-2023

What is New in this Guideline?

Terminology	**TLD 1** (or ALD 1 in children)	Clients on a DTG-containing regimen, who have **never failed** any other regimen (previous "first-line" terminology)
	TLD 2 (or ALD 2 in children)	Clients on a DTG-containing regimen, who **have failed** an earlier regimen (previous "second-line" terminology)
	Dispensing cycle:	A dispensing cycle (DC) is defined as the number of days for which a client would have treatment if a single standard "monthly" quantity of tablets were dispensed. The term DC is preferred to the previously used term 'month' due to the potential discrepancy that may arise between the days of treatment dispensed (if 28-day pack sizes are used) and the days in a month (on average, 30 days)
ART Regimens	**All adult and adolescent clients > 30 kg and > 10 years of age, including pregnant and breastfeeding women**	• The preferred first-line ART regimen is **tenofovir disoproxil fumarate-lamivudine- dolutegravir (TLD)** for those adult and adolescent clients initiating ART. • TDF weight-related eligibility criteria decreased from **35 kg to 30 kg** • All clients already on ART and not on dolutegravir (DTG), whether on first-line or second-line regimens, should be evaluated for a switch to a dolutegravir-containing regimen.
		• TDF may safely be reused in 2nd-line therapy following 1st-line failure with TDF-containing regimens. TLD will therefore be used as both first (TLD 1) and second (TLD 2) line regimens and in certain cases, 3rd line regimens as well • Simplified **switching from TEE to TLD not dependant on VL**
	New formulations	• **DTG 10 mg dispersible tablets** for children from ≥ 3 kg and ≥ 4 weeks of age • DTG-containing fixed-dose combination: Abacavir (ABC) 600 mg + lamivudine (3TC) 300 mg + DTG 50 mg (ALD FDC). ALD FDC can be prescribed for clients ≥ 25 kg
	Children ≥ 3 kg and ≥ 4 weeks of age until 29,9 kg or 9 years of age	• The preferred first-line ART regimen is **abacavir-lamivudine-dolutegravir (ALD)**. • All paediatric clients already on ART and not on dolutegravir (DTG), whether on first-line or second-line regimens, should be evaluated for a switch to a dolutegravir-containing regimen.
	Other antiretrovirals	• **Abacavir** is the preferred alternative agent if TDF cannot be used • Zidovudine (AZT) no longer part of any standard ART regimen. AZT will be reserved only for cases with **both** renal failure **and** ABC hypersensitivity • **Atazanavir/r** replaces lopinavir/r as the preferred protease inhibitor except when on TB treatment
Monitoring on ART	**VL monitoring**	**First VL** after ART initiation to be done after 3 dispensing cycles
	Creatinine and eGFR	eGFR previously done at 'month' 6 moves to 'month' 3 (i.e. after 3 dispensing cycles) to align with the new VL monitoring schedule
Virological Failure	• **Definition:** two or more VLs ≥ 1000 c/mL taken two or more years after starting a DTG/PI-containing regimen and adherence > 80% • **Focus on improved adherence:** Resistance to DTG is very uncommon. If other reasons for an unsuppressed VL (including drug interactions) have been addressed or excluded, 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. • **No regimen changes without a resistance test:** Switching off a DTG-containing regimen should only happen if InSTI resistance has been confirmed by a resistance test • Resistance testing can only be authorised by a member of the National Third-line committee, one of the helpline consultants, or a nominated provincial expert	

Other updates	• 2 high quality counselling sessions at ART start and at follow-up a month later
	• Reduces health facility visits in the first year on ART to support continued engagement in care, including visit schedule for first year on treatment.
	• Removes time on ART from repeat prescription collection strategies (RPCs) eligibility criteria, enabling access as soon as first VL is suppressed.
	• Reduces visits once enrolled in RPCs with a maximum of 2 visits per 6-month scripting cycle.
	• Returns clients in RPCs with VL 50-1000 c/mL to clinician care for TLD switch and VL management
	• Enables multi-month dispensing (MMD) by the facility between clinical visits including for people not eligible for RPCs - children from 6 months of age, post-natal women, people co-infected with TB, with elevated viral loads or re-engaging in care.
	• Introduces a differentiated approach to management on re-engagement.
	• Integrates contraception and TB preventative therapy into all service delivery models
	• Aligns ART visit schedules to TB management and infant EPI schedules to enable integration
	• Incorporates tools for:
	  • enhanced adherence counselling
	  • mental health assessment	

Overview

This ART Clinical Guideline is intended to serve as a quick reference guide for antiretroviral treatment (ART) in adults, pregnant and breastfeeding 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.

These guidelines have been revised with the Differentiated Models of Care (DMOC) Standard Operating Procedures (SOPs) to ensure simultaneous consideration and alignment of clinical, adherence and service delivery updates. The DMOC SOPs form part of this guidance to enable optimal use of decentralised and integrated service delivery and should be read concurrently with this clinical guideline.

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
- Provide guidance on routine management of clients on ART to promote viral suppression
- Highlight critical areas for provision of integrated ART, TB, and family planning services, and the use of differentiated models of care

The preferred first-line ART regimen is tenofovir disoproxil fumarate-lamivudine-dolutegravir (TLD) for those adult and adolescent clients initiating ART, and abacavir-lamivudine-dolutegravir (ALD) in children . All clients already on ART and not on dolutegravir (DTG), whether on first-line or second-line regimens, should be evaluated for switch to a dolutegravir-containing regimen.

In the new ART era of dolutegravir, TLD will be used as a first-line and a second-line ART regimen, and as part of certain third-line regimens with other medicines. This has necessitated a change of the previous "first-line" and "second-line" terminology to the following:

TLD1: Clients on a DTG-containing regimen, having never failed a previous regimen (old "first-line" terminology)

TLD2: Clients on a DTG-containing regimen, who have failed a previous regimen (old "second- line" terminology)

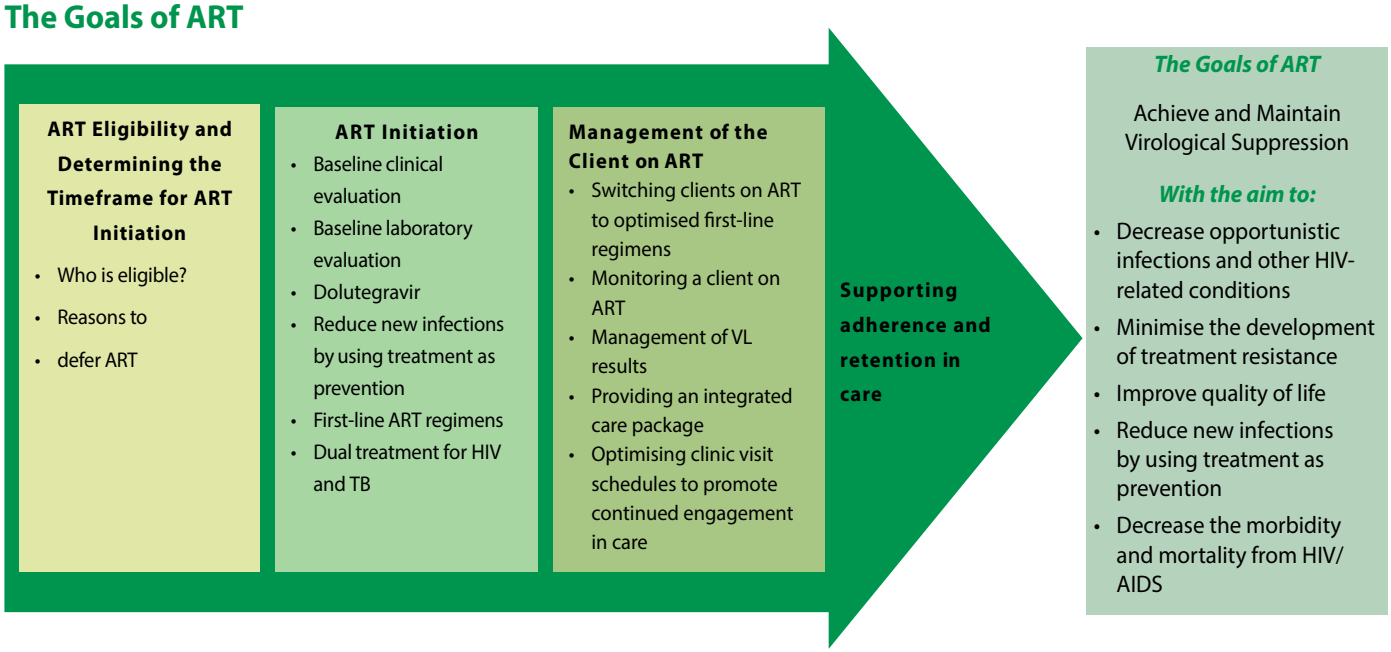
The safety of DTG in women of childbearing-potential has been firmly established and neural tube defects are no longer a concern that influences regimen choice in women. However, the integration of family planning and ART services remain of paramount importance, and issues of family planning and contraception should be discussed at every clinical interaction to understand the client's current fertility desires and healthcare needs.

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. All individuals should be assessed for advanced HIV disease (AHD) and provided with a comprehensive package of care, including cotrimoxazole prophylaxis, as needed.

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, sustained viral suppression 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. Many 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 ART initiation is encouraged where possible, all clients, particularly those with advanced HIV disease, should be carefully assessed for opportunistic infections (OIs) 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 symptomatic clients 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: • 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 • If CD4 ≥ 50 cells/µL – initiate ART 8 weeks after starting TB treatment • In pregnant and breastfeeding women (PBFW) initiate ART within 2 weeks of starting TB treatment, when the client's symptoms are improving, and TB treatment is tolerated. Defer ART for 4–6 weeks if symptoms of meningitis are present. For further details, refer to the Family-Centered Transmission Prevention Guideline 2023
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 and if lumbar puncture is (LP) negative for cryptococcal meningitis (CM)	No need to delay ART. ART can be started immediately.
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 TB, 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**.

Interventions to support adherence to ART

ART literacy education and fast-track initiation counselling (FTIC) empower clients to adhere to treatment, and positively influence clinical outcomes. Adherence counselling at ART initiation and first follow-up visit should focus on:

- providing the client with an understanding of HIV, ART, and the importance of VL suppression
- providing the client with practical skills to adhere to ART
- identifying any potential risk factors for adherence in the future
- An individualized adherence plan should be developed with clear treatment milestones, including an undetectable viral load

The minimum components of the baseline clinical evaluation are outlined in the following table:

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 See also the section on ***"Advanced HIV Disease" in the 2023 Consolidated ART Guideline***	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. To identify underweight/ obese clients requiring nutritional and lifestyle support	Measure weight and height and determine BMI (kg/m^2): < 18.5 = underweight; 18.5 to 25 = normal; > 25 to < 30 = overweight; ≥ 30 = obese	Measure mid upper arm circumference (MUAC) 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
Test for TB	To identify clients who require treatment for TB To identify clients who do not have active TB and who may be eligible for TPT ***see "TB Preventive Therapy" on page 9***	At enrolment into care/ ART start: • TB symptom screen and clinical examination • Routine MTB/Rif Ultra (Xpert) on all PLHIV at enrolment into ART care (regardless of TB symptoms)	For all HIV-positive women at first visit in antenatal clinic, do a: • TB symptom screen and clinical examination • Routine MTB/ Rif Ultra (Xpert) (regardless of TB symptoms)	Identify symptoms of cough, night sweats, fever, failure to thrive as outlined in the TB screening tool Attempt sputum testing (and Xpert) where feasible Enquire about TB contacts

Additional TB Investigations for Symptomatic Clients:

For symptomatic PLHIV admitted to hospital [in addition to the MTB/Rif Ultra (Xpert)]
• Do a U-LAM test
• Do a chest X-ray if clinically indicated
• Do other investigations for extra-pulmonary TB if clinically indicated
 	
Enquire about TB contacts
	For symptomatic PLHIV seen in an outpatient setting [in addition to the MTB/Rif Ultra (Xpert)]
	• Do a U-LAM test if:
	  • CD4 count <200 within the last 6 months, or
	  • advanced HIV disease, or
	  • current serious illness.
	• Do a chest X-ray if clinically indicated

Component of the Baseline Clinical Evaluation continued	Purpose	Further Action Required		
		Adolescents (10–19 years) and Adults	Pregnant Women	Children (< 10 years)
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. Do/refer the client for a **lumbar puncture**. Defer ART if meningitis is confirmed as outlined in ***"Medical Indications to Defer ART" on page 4***		
Screen for active depression, other **mental health** issues or substance abuse	Mental health conditions and substance use can affect adherence and the client's quality of life. In general, ART can be initiated, and cautiously monitored see also ***"Mental Health Assessment" on page 31***	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. 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 vertical transmission. 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: "Do you have any genital discharge?" "Do you have any genital ulcers?" "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:** **At ART initiation**, WHO clinical stage helps us to: Understand the severity of the client's clinical condition and the associated risk of mortality Determine the urgency and timing of ART initiation Determine if cotrimoxazole prophylaxis (CPT) is indicated see ***"Indications for Starting and Stopping Cotrimoxazole Preventive Therapy" on page 8***			

Baseline Laboratory Evaluation for Adults and Adolescents, Pregnant Women, and Children

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 Preventive Therapy" on page 8***		
	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 8***		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. 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] Children ≥ 5 years: Do FBC. Characterise according to MCV and manage accordingly[1]
GeneXpert (MTB/Rif Ultra)	To diagnose TB	For any client with a positive TB symptom screen For people living with HIV, regardless of TB symptoms: At the time of HIV diagnosis On enrolment in antenatal care for pregnant women		
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 If CrAg-negative, no fluconazole is required If CrAg-positive, the client will require treatment of the infection 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" on page 23***	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 the cervical screening results suggest a possible abnormality of the cervical cells, then a clear plan for further investigation and treatment (e.g. colposcopy and LLETZ procedure) should be determined according to the local referral guidelines.	Pregnancy does not preclude screening for cervical cancer and it can be performed up to 20 weeks of gestation. If the cervical screening results suggest a possible abnormality of the cervical cells, then a clear plan for further investigation (e.g., colposcopy) should be determined according to the local referral guidelines	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 2020

Assessing Renal Function

! A low absolute creatinine level is of no concern and needs no intervention. It may be an indication of low muscle mass. However, a low creatinine clearance (eGFR) is of concern and indicates reduced renal function.

Assessing Renal Function			
Age/pregnancy Status	**What must be measured?**	**Acceptable level for TDF use**	**Counahan Barratt formula** $\text{eGFR (mL/min/1.73 m}^2\text{)} = \frac{\text{height [cm]} \times 40}{\text{creatinine [µmol/L]}}$
≥ 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/1.73m^2	
Pregnant women	Absolute serum creatinine level	< 85 µmol/L	
DTG is known to decrease tubular secretion of creatinine without affecting glomerular filtration. Serum creatinine concentrations 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.			

[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" on page 23.*** 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 through a clinical evaluation and by testing for TB. If the client is asymptomatic, TPT initiation need not be delayed if TB GeneXpert results are outstanding. TPT and ART can be initiated on the same day. A Tuberculin skin test (TST) is not required prior to starting TPT. TB testing strategies will vary by age as younger children cannot spontaneously expectorate sputum. In well children without symptoms, neither sputum testing nor CXR are therefore requirements to start TPT. Sputum testing should be attempted in children who can expectorate spontaneously (typically > 25kg), but if they are well (without symptoms) and unable to expectorate, they should start TPT, even if no CXR or sputum testing is available.

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 (12H) and pyridoxine 25 mg daily Rifapentine and isoniazid weekly (3HP) may be available in selected locations*
Children living with HIV who are < 15 years of age	• Children undergoing their first evaluation for HIV and ART, from 14 weeks of age • All children (including neonates) with significant exposure to TB	Isoniazid, oral, 10 mg/kg/day for 6 months (maximum dose 300 mg daily) and pyridoxine daily
Pregnant women	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

* Alternative TPT regimen for adults, adolescents and children ≥ 25 kg: Where available, 3HP (weekly isoniazid and rifapentine) can be used in clients on a DTG-containing regimen who have a VL < 50 c/mL in the last 6 months. 3HP should NOT be used in new clients initiating a DTG-containing regimen. In these clients, 12H is still the preferred TPT regimen. Where 12H/3HP is prescribed for a client in an RPCs, no additional clinician review visits are required (the full 3 months 3HP supply/6 months of 12H can be scripted).

Dolutegravir

For further detail on switching **existing stable clients on ART** between regimens, see ***"Switching existing clients to DTG-containing regimens" on page 14***

Dolutegravir (DTG) Overview

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 clients 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
- Abacavir (ABC) 600 mg + lamivudine (3TC) 300 mg + DTG 50 mg (ALD). ALD can be prescribed for clients ≥ 25 kg
- DTG 50 mg tablet
- DTG 10 mg dispersible tablet
- Please note that the adult film coated 50 mg tablet and the paediatric dispersible 10 mg tablet are not bioequivalent. The 50 mg film coated tablet is the equivalent of 30 mg of the dispersible tablets.

Standard Dose: Children ≥ 20 kg; adolescents and adults: DTG 50 mg daily
Children > 4 weeks of age and 3–19 kg: As per ***"Drug Dosing Chart" on page 34***

DTG dose with concomitant rifampicin-containing TB treatment: Increase DTG dose to 50 mg 12-hourly. If on TLD or ALD FDC, add DTG 50 mg 12 hours after TLD or ALD dose. If on paediatric DTG, follow ***"Drug Dosing Chart" on page 34*** for DTG and concomitant rifampicin-containing TB treatment

Side-effects: Usually mild and self-limiting. Side-effects include insomnia, headache, central nervous system (CNS) effects, and gastrointestinal effects. 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.

Contrary to initial speculation that the integrase inhibitor class may be causing **weight gain**, the association now appears not to be causal. Instead, the association may be the result of comparatively less metabolic toxicity than alternative older ART regimens (that mitigate weight gain through toxicity) combined with an initial return-to-health phenomenon, and an obesogenic environment. Dolutegravir-based ART regimens have numerous advantages over comparators and are still recommended first-line agents for people living with HIV. There is no role for switching from dolutegravir-containing regimens in patients gaining weight.

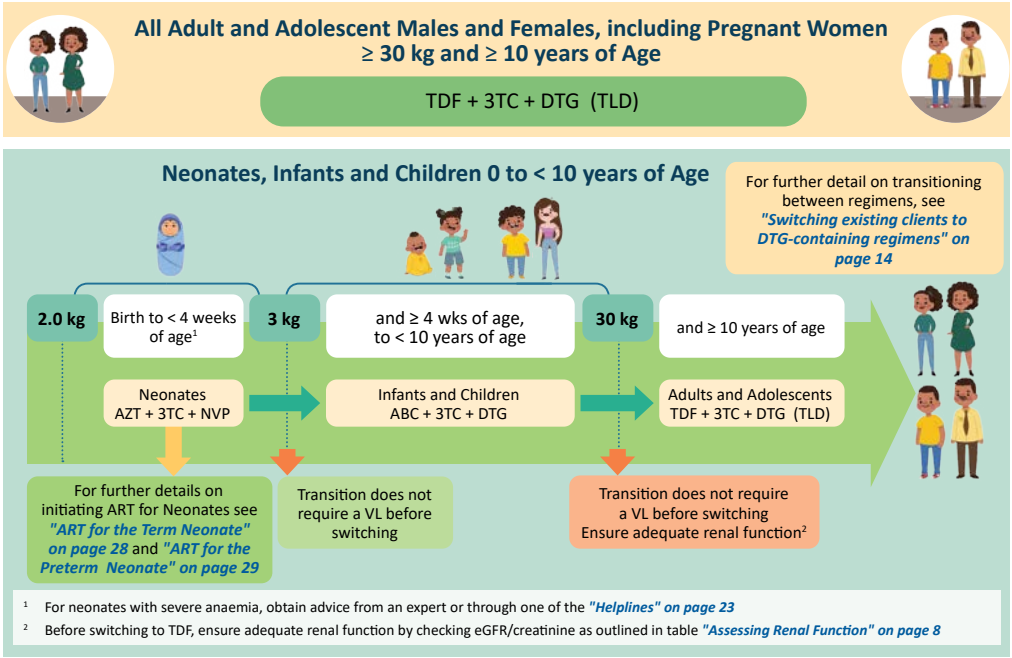
Drug Interactions with Dolutegravir

!	Drug interactions can result in suboptimal drug concentrations which can cause • an elevated HIV viral load • drug resistance, due to replicating virus in the presence of subtherapeutic drug concentrations • For interactions with paediatric regimens see *"Drug Interactions with DTG and Rifampicin-containing TB Treatment" on page 13*

Interacting Drug[1]	Effect of Co-Administration	Recommendation
Rifampicin	↓ Dolutegravir	Increase DTG dose to 50 mg 12-hourly. If on TLD FDC, add DTG 50 mg 12 hours after TLD dose. For interactions with paediatric regimens see *"Drug Interactions with DTG and Rifampicin-containing TB Treatment" on page 13*
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. It is safe to dissolve the DTG dispersible tablets in breast milk. 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. 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
	* Many over the counter (OTC) medications contain polyvalent cations. Clinicians should regularly ask clients about OTC medication use and advise about possible interactions	
Anticonvulsants: • Carbamazepine • Phenobarbital • Phenytoin	↓ Dolutegravir	Avoid coadministration if possible. Alternative agents that do not interact with DTG include valproate, lamotrigine, levetiracetam, and topiramate. Remember that valproate is contra-indicated during pregnancy. 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 concentrations. Maximum metformin dose 500 mg 12-hourly

[1] This table includes some of the most important drug interactions with DTG. 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" on page 23*

First-Line ART Regimens in Adults, Adolescents, Pregnant Women, Children, Infants, and Neonates



[1] For neonates with severe anaemia, obtain advice from an expert or through one of the *"Helplines" on page 23*

[2] Before switching to TDF, ensure adequate renal function by checking eGFR/creatinine as outlined in table *"Assessing Renal Function" on page 8*

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 information on different contraceptive methods available. 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. Also provide her with information on infant feeding, infant HIV prophylaxis, and follow-up infant HIV testing. Provide a 2-month supply of her ART regimen at discharge from labour ward (see DMOC SOP 4).

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[3], family planning services should continue to be offered with ART and child health services in an integrated and patient-centred manner. This is especially urgent if the women's VL is not suppressed.

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.

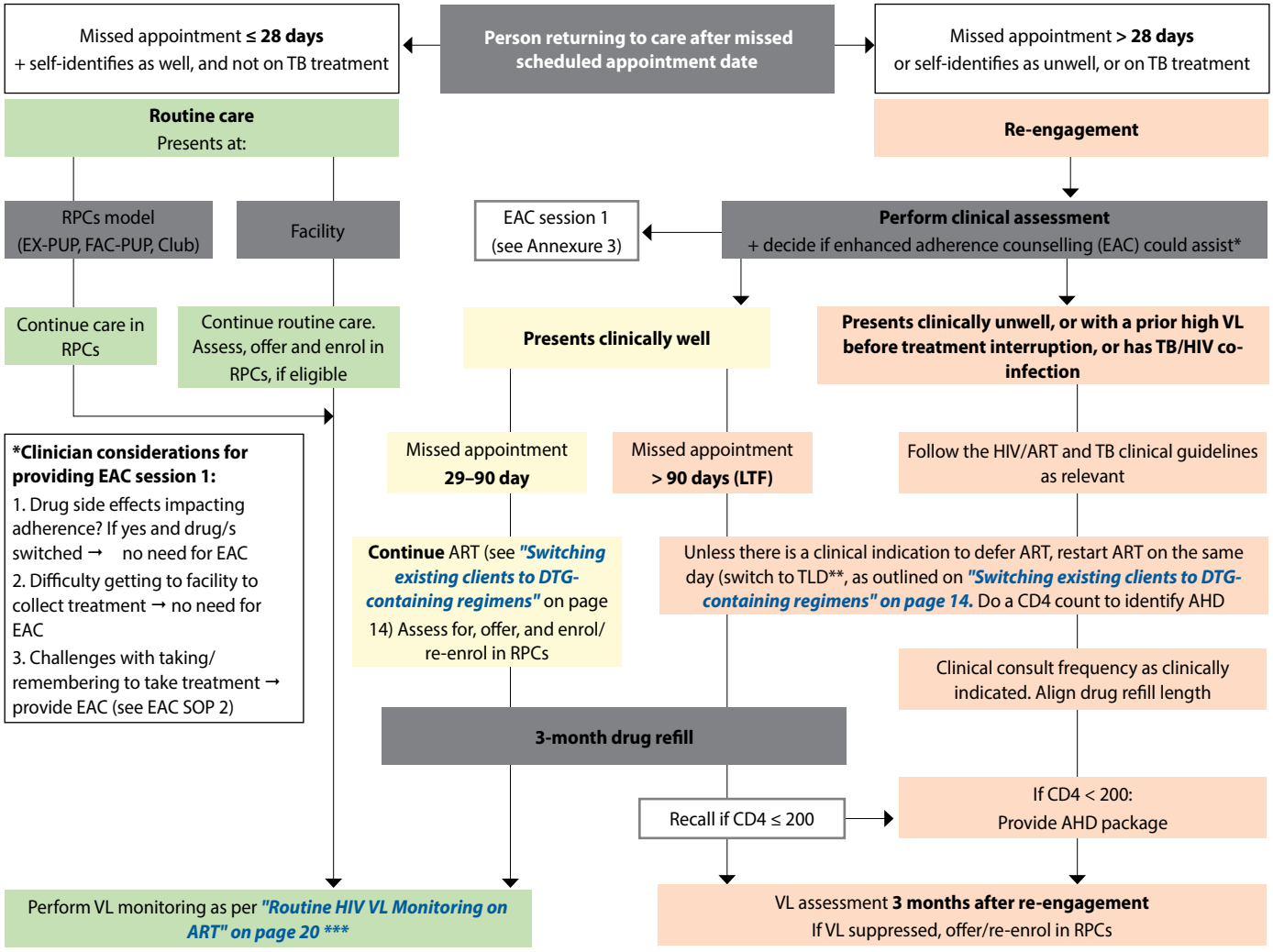
Contraceptive choices need to respect and fulfill human rights and enable clients to make informed choices for themselves. Client contraceptive choices, however, are often influenced directly or indirectly by social, economic and cultural factors. It is in this context that clients should be given comprehensive, scientifically accurate information in order to assist them to make an informed, voluntary choice of a contraceptive method. A woman's choice of contraceptive method may be influenced by her ART service delivery model to allow for better visit alignment. See also the ***"Visit Schedule for Integrated Care for Clients on ART and Drug-Sensitive TB Treatment" on page 26***

Should a woman desire pregnancy, counsel her regarding optimal timing for a healthy pregnancy. Recommend that ART is established, viral suppression is attained, and that she has no current OIs before she tries to become pregnant.

Issues of family planning and contraception should be discussed at every clinical interaction.
Where feasible, every attempt should be made to provide ART and family planning from the same service delivery point

[3] NDoH NEMLC PHC-Adult Medicine review DTG in Pregnancy 17June 2021

Re-initiating ART in Non-pregnant Clients who have Interrupted Treatment



AHD = Advanced HIV Disease; EX-PUP = External pick-up point; FAC-PUP = Facility pick-up point; RPCs = Repeat Prescription Collection Strategies

** All clients returning to care after > 90 days, and who were previously on TEE, TLD, or a PI-based regimen, should re-initiate a DTG-containing regimen. Clients who became LTFU on third-line should re-initiate their third-line regimen

*** Where the patient is overdue for their routine assessment at return, only perform the assessment once the patient has taken treatment for 3 months (or if in RPCs, the closest clinical review date thereafter).

Co-treatment of HIV and Active TB in Neonates, Infants, Children, Adolescents and Adults

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

1. **The timing of ART initiation** *see"Medical Indications to Defer ART" on page 4*
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

Clients who are not yet on ART when TB treatment is initiated

- Children and adolescents should initiate ART with a DTG-containing regimen, with boosting of DTG as explained below.
- Adults should initiate ART with either:
  i. a DTG-containing regimen, with boosting of DTG as explained below, or
  ii. an EFV-containing regimen, provided the client is ART treatment-naive. EFV has no significant drug interaction with rifampicin and has the benefit of being a once-daily regimen which supports adherence.

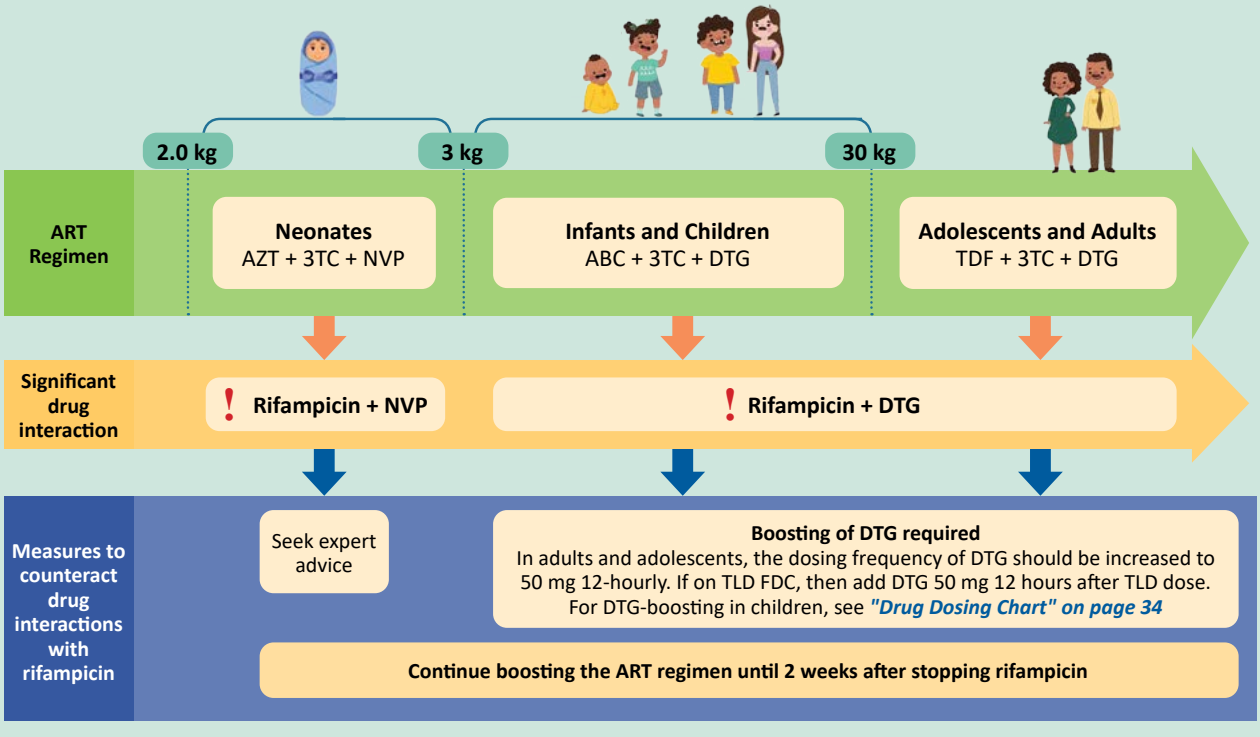
Clients who are already on ART when TB treatment is initiated

- All clients who are already on a DTG-containing regimen when TB treatment is initiated should continue the DTG-containing regimen whilst also taking TB treatment, with boosting of DTG as explained below.
- Clients who are already virally suppressed on an EFV-containing regimen when TB treatment is initiated should continue the EFV-containing regimen whilst also taking TB treatment. The EFV-containing regimen should be continued until two weeks after TB treatment is completed. Thereafter, EFV can be switched to DTG.

! Clinicians should provide integrated TB and ART management at clinical consultation visits. Failure to combine care leads to increased visits and significantly increases the risk of disengagement. See also *"Integrated Visit Schedule for Clients on ART and Drug-Sensitive TB Treatment" on page 26*

Drug Interactions with DTG and Rifampicin-containing TB Treatment

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 Protease Inhibitors, e.g., Lopinavir/ritonavir

Every effort should be made to switch clients to DTG-containing regimens. However, during the transition process, some clients may still be on PI-containing regimens and may also require TB treatment. Rifampicin cannot be given with ATV/r or DRV/r. Significant drug interactions between LPV/r and rifampicin should be managed as follows:

LPV/r tablets: Double-dose LPV/r tablets in adults, adolescents and children able to swallow whole LPV/r tablets. See *"Drug Dosing Chart" on page 34*. Tablet must not be crushed, broken or chewed. If the client is unable to tolerate LPV/r at double doses, consult one of the *"Helplines" on page 23*.

LPV/r solution or pellets or 4 in 1 (ABC/3TC/LPV/r): Super-boosting with additional ritonavir powder: maintain standard LPV/r dose but add additional ritonavir twice daily as per *"Drug Dosing Chart" on page 34*. If no powder is available, consult an expert for a suitable alternative. Ritonavir powder has a shelf-life of 36 months. Note that ritonavir 100 mg tablets must not be crushed, broken or chewed.

Optimising Regimens and Visit Schedules for the Client on ART

Switching Existing Clients to DTG-containing Regimens (Adults, adolescents or children)

Non VL-dependent regimen switches 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** ABC/3TC/EFV (or NVP*) AZT/3TC/EFV (or NVP*) AZT/3TC/DTG Any LPV/r or ATV/r regimen for **less than 2 years**	**Switch all to a DTG-containing regimen, regardless of VL result** Review VL in last 12 months. 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. If VL was not done in last 12 months, do it at this visit, but do not wait for the result to switch	**TLD** provided no renal dysfunction and age ≥ 10 yrs and weight ≥ 30 kg If client does not qualify for TDF **ABC[1]/3TC/DTG** If client does not qualify for TDF and has ABC hypersensitivity **AZT/3TC/DTG**

! * There should no longer be any client (older than one month and > 3 kg) using a NVP-containing treatment regimen.
Clients who previously used NVP as an alternative to EFV for psychiatric reasons, should be switched to DTG as a matter of urgency

Be sure to check for possible drug interactions when switching to DTG and manage as per ***"Drug Interactions with DTG and Rifampicin-containing TB Treatment" on page 13***

! Clients on TEE and receiving treatment through an RPCs can be switched to TLD at their next re-scripting visit and can remain in their RPCs, provided they have a VL < 50 c/mL in the last 12 months. No additional facility visits are required (see DMOC SOP 6).
Any client in an RPCs with a VL ≥ 50 c/mL in the last 12 months, should be recalled to the facility for further clinical management. If the client is on TEE, continue to switch same day to TLD, but do an ABCDE assessment and provide enhanced adherence counselling (EAC) if indicated. If clinically well, 3MMD can be provided by the facility until the repeat VL assessment (see DMOC SOP 4) in 3 months, as per ***"VL Monitoring for Clients on TLD" on page 21***. Review the repeat VL result. If suppressed again, re-enrol in RPCs. If the VL remains unsuppressed, manage as per the ***"VL Monitoring for Clients on TLD" on page 21***. Clients with clinician confirmed low-level viraemia can be re- enrolled in RPCs.

Switching Existing Clients to DTG-containing Regimens (Adults, adolescents or children who have never used a DTG-containing regimen in the past)

[1] If clients are not eligible to use TDF and they had an ABC hypersensitivity reaction, use AZT/3TC/DTG

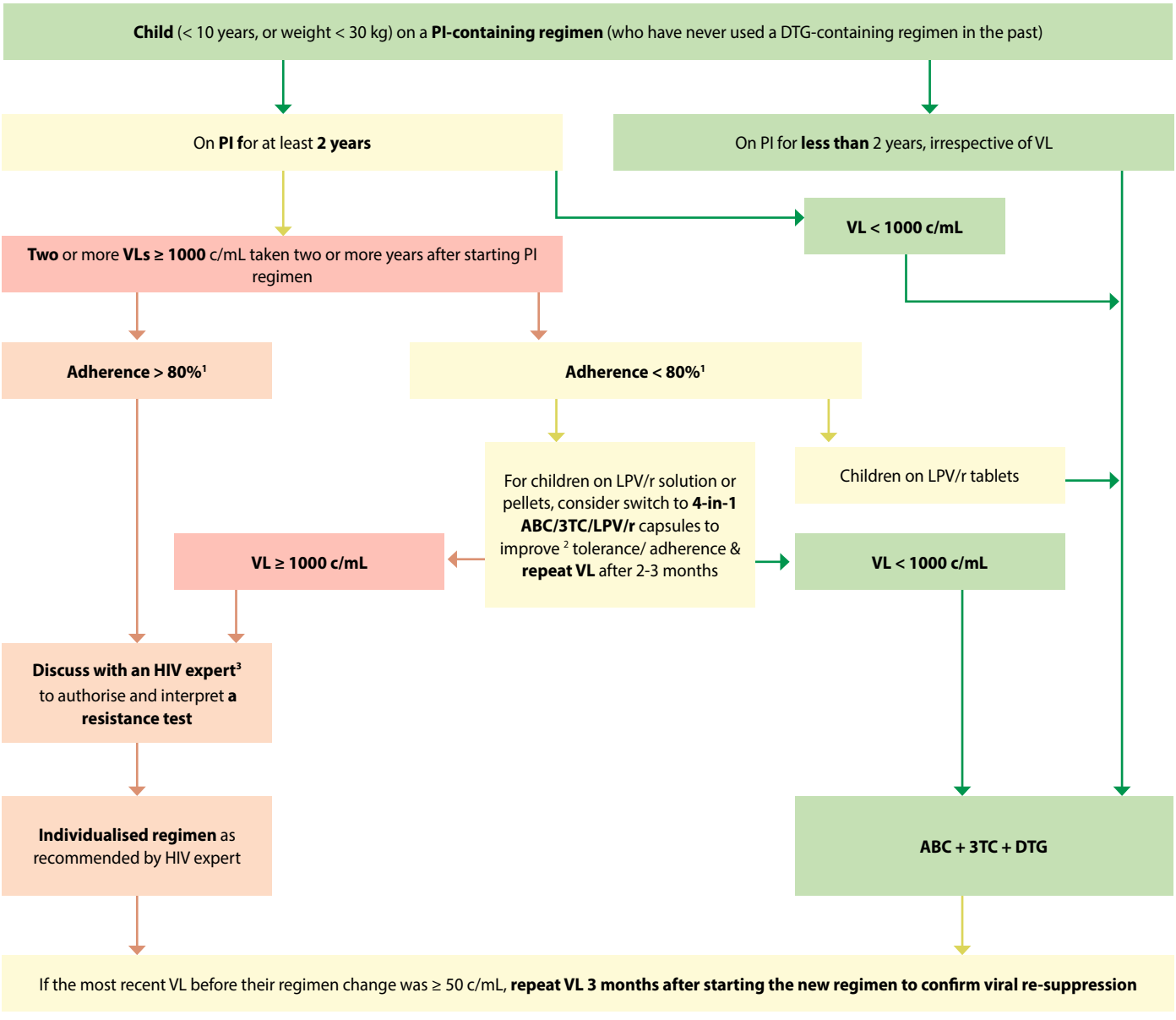
VL-dependent regimen switches Relevant to all clients who have been on PI-based regimens for more than two years: their VL result in the last 12 months will influence the decision of how and when to switch to a DTG-containing regimen			
VL considerations	**Current Regimen**	**Criteria for switch**	**Regimen 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** If VL in last 12 months was ≥ 50 c/mL, continue to switch same day, but do ABCDE assessment, provide EAC if needed, and repeat the VL after 3 months as per ***"The VL non-suppression algorithm" on page 21***	**TLD** provided no renal dysfunction and age ≥ 10 yrs and weight ≥ 30 kg If clients does not qualify for TDF ABC[1]/3TC/DTG
[2] **Two or more consecutive VLs ≥ 1000 c/mL** taken **two or more years** after starting PI regimen	Adult or adolescent on any **LPV/r or ATV/r** regimen and adherence **less than 80%**[3]	**Switch all to a DTG-containing regimen** **Do not do a resistance test** 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. Manage as per ***"The VL non-suppression algorithm" on page 21***	**TLD** provided no renal dysfunction and age ≥ 10 yrs and weight ≥ 30 kg 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 and have confirmed adherence more than 80% may need a resistance test. **These clients do not qualify for a same-day switch.** Discuss with an HIV expert[4] to authorise and interpret a resistance test. Provide individualised regimen as recommended by HIV expert. Repeat VL 3 months after the regimen change to confirm re-suppression, as per the ***"Management of Confirmed Virological Failure on TLD" on page 23***	
	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. Refer to algorithm ***"Switching children on PI-containing regimens to DTG- containing regimens" on page 16***	

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 [e.g. TFV urine lateral flow assay (LFA) for presence of TDF in urine, TFV diphosphate (detects TDF on dried blood spot samples), DTG plasma levels]

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



1. Although objective measures of poor adherence include pharmacy refills or 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
2. If a switch to the 4-in1 capsules does not improve adherence, or is not available, continue to switch to ABC + 3TC + DTG as for non- adherent children on LPV/r tablets
3. The following would qualify as HIV experts: the HIV Helplines, a paediatric infectious disease specialist or the paediatric Third line ART committee

Summary of the Care Continuum for Clients 5 years of age and older 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 one month after starting ART, only need to be seen again 2 months later for clinical review and their first viral load and serum creatinine. 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), 3) not having any other uncontrolled chronic conditions that require clinical review more frequently than 6-monthly, and 4) not being pregnant.

The diagram ***"Visit Schedule for Adults, Adolescents and Children 5 Years and Older on ART" on page 18*** 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 repeat prescription collection strategies (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 DMOC standard operating procedure (SOP) 5 (facility-pick-up points, adherence clubs and external pick-up points).

See also ***"Visit Schedule for Integrated Care for Clients on ART and Drug-Sensitive TB Treatment" on page 26*** and ***"Visit Schedule for Integrated Care for the Mother-baby Pair Living with HIV" on page 24***

! If a patient comes from a different facility, it is critical that the patient be provided with treatment on the day of presentation to limit any further treatment interruption and its impact on viral suppression. While referral letters are helpful, a patient cannot be required to leave the facility without treatment to first obtain a referral/transfer letter.

Women with contraceptive needs should have contraceptive method options explained, specifically how each method impacts all required return visits' location (facility or outside of the facility) and visit frequency:

- Long-acting reversible contraception (LARC) removes any increased visit frequency or alignment concerns.
- The combined oral contraceptive pill (COCP) can be repeated 3-monthly, aligns well with ART and well-baby visit schedules (if applicable), and can be scripted through her preferred RPCs.
- The DMPA 3-monthly injection must be administered by a clinician but aligns with ART and well-baby visit schedules
- The NET-EN 2-monthly injection also needs to be administered by a clinician, but will require additional visits by the mother.
- Where a woman chooses to continue clinician administered short-acting injectable contraception (e.g., DMPA or NET-EN), a facility-based pick-up point (FAC-PUP) or facility-based adherence club may be the preferred option provided visit alignment can be ensured.

HELPLINES

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**

Visit Schedule for Adults, Adolescents and Children 5 Years and Older on ART

DC/ Months* on ART	Routine monitoring tests	Overview of Management
0	**Baseline clinical and lab assessment as outlined on pages 4 to 6 ART initiation and session 1 of fast track initiation counselling**	
1	**Review test results**	• Session 2 of fast track initiation counselling including planning for travel and VL education • Clinical assessment and routine monitoring as outlined on page 19 • Integrated services for family planning and NCDs • **2 months ART dispensed (2MMD) - DMOC SOP 4**
3	**3-month* VL sCR and eGFR**	• Clinical assessment including VL and any other routine • monitoring bloods as outlined on page 19 • • Integrated services for family planning and NCDs

4	**Review test results**	• Clinical assessment and review of VL and any other monitoring results
		• Integrated services for family planning and NCDs
		• Assess eligibility for Repeat Prescription Collection strategies (RPCs) (South Africa's differentiated models of care for stable patients)
		  • VL < 50 c/mL
		  • Clinically well
		  • No OIs, including TB
		  • Not pregnant
		Repeat Prescription Collection strategies (DMOC for stable patients)
		Facility Pick-up Point (FAC-PUP) (DMOC SOP 5.1) | Adherence Clubs (AC) Facility or community-based support groups (DMOC SOP 5.2) | External Pick-up point (EX-PUP) (DMOC SOP 5.3)
		• Renew prescription for next 6 months, with first 3 month's supply issued today from the facility
		• If not eligible for RPCs or refused RPCs:
		Assess eligibility for facility provided multi-month dispensing (MMD) – DMOC SOP 4

7		• Collect medication from preferred RPCs
10	**10-month* VL sCR and eGFR CD4 count**	• Clinical assessment including VL and any other monitoring bloods as per ***"Monitoring on ART" on page 19*** • Integrated services for family planning and NCDs • Check TPT eligibility • Renew prescription for next 6 months • Do not require clients to return to the facility in 1 month to review the VL results, unless other clinical indications exist that require review. Rather, recall to the facility only those clients with elevated VLs
11+		• 12-monthly clinical assessment and family planning review as per ***"Monitoring on ART" on page 19*** • 12-monthly routine monitoring of VL, sCR and eGFR • Check that chosen RPCs option is still suitable • Collect medication from preferred RPCs

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) (see also ***"Re-engagement algorithm" on page 12***)
- a VL ≥ 50 c/ml
- possible signs or symptoms of clinical failure, e.g. if the client is acutely unwell, or develops a new OI such as TB

A clinician should:

- If in an RPCs, return the client to regular care to ensure more frequent clinical follow-up until they are stable again.
- Provide appropriate clinical management
- If clinically well and struggling with visit frequency: provide multi-month dispensing (DMOC 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)

! Clients on TEE and receiving treatment through RPCs can be switched to TLD and remain in their RPCs if they have a VL < 50 c/mL in the last 12 months.

*The term dispensing cycle (DC) is defined as the number of days for which a client would have treatment if a single standard "monthly" quantity of tablets was dispensed (usually 28 days). Although it is understood that the time frame for a month and a DC are not necessarily the same, for ease of reading, the term 'DC' and 'month' are used interchangeably in this table, and should be considered synonymous.

Managing the Client on ART

Monitoring on ART

! Remember to check adherence at every clinical follow-up visit, in a non-judgemental way. Ask open ended questions e.g. "Is there anything that makes it difficult for you to take your treatment?" See also the 'Adherence' section of the ***"ABCDE assessment of an Elevated Viral Load" on page 22***

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:**	**Viral load** should be measured to timeously detect problems with adherence or treatment failure	**Side-effects and ART toxicities** can affect adherence and endanger the client's health:
Weight (adults) An assessment of trends in weight in adults	! Remember, any elevated VL > 50 c/mL is a medical emergency! Assess and manage according to the algorithm ***"VL Monitoring for Clients on TLD" on page 21***	**Drug side-effects** Ask about side-effects at each visit (e.g. sleep or gastrointestinal disturbances)
Growth and neurodevelopment (children) An assessment of trends in weight, height, head circumference, and neurodevelopment ! Remember to increase the ART dosage as weight increases!	**The CD4 count** monitors susceptibility to opportunistic infections, identifies clients with advanced HIV disease and informs eligibility for OI prophylaxis.	**TDF-induced nephrotoxicity** If on TDF, do creatinine and eGFR* at months 3 and 10 (aligned with VL monitoring schedule) Thereafter, repeat every 12 months See also ***"Assessing Renal Function" on page 8***
Screen for TB (see below *) **and other OIs:** to diagnose and provide treatment; to adjust ART regimen if required; to provide a package of care for AHD if required; to determine if TB preventive therapy is required	Monitor routinely after 10 months/DCs on ART (aligned with VL). Thereafter, stop CD4 monitoring unless: • CD4 still ≤ 200 cells/mm^3: repeat every 6 months until CD4 > 200 • VL ≥ 1000 c/mL: repeat CD4 every 6 months until VL < 1000 c/mL • A clinical indication arises, such as a new WHO Stage 3 or 4 condition in a previously well client Repeat CD4 for clients returning > 90 days after missing a scheduled appointment (see ***"re-engagement algorithm" on page 12***)	**Dyslipidaemia** If on a PI-based regimen, 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
WHO clinical staging to determine response to ART, and CPT eligibility		**Anaemia and neutropaenia** If on AZT, do a full blood count and differential white cell count at months 1 and 3 Thereafter, repeat if clinically indicated
Screen for pregnancy and ask if planning to conceive as outlined in the table for ***"Baseline Clinical Evaluation" on page 5***		

* Screening for TB at follow-up Visits

At every routine follow-up visit:	At every 12-monthly clinical review on ART (aligned with 12-monthly VL)	For symptomatic PLHIV admitted to hospital [in addition to the MTB/Rif Ultra (Xpert)]	For symptomatic PLHIV seen in an outpatient setting [in addition to the MTB/Rif Ultra (Xpert)]

• Do a TB symptom screen. If symptomatic, do a MTB/Rif Ultra (Xpert)	• Routine MTB/Rif Ultra (Xpert) (regardless of TB symptoms)	• Do a U-LAM test	• Do a U-LAM test if:
			  • CD4 count <200 within the last 6 months, or
			  • advanced HIV disease, or
			  • current serious illness.

For more information on the package of care for AHD and the management of specific OIs, please refer to the ***Consolidated ART guideline***

! When monitoring on ART, also integrate monitoring for other chronic conditions (HPT, DM, and mental health) and routinely offer reliable contraception and cervical cancer screening to female clients.