



# 2019 ART Clinical Guidelines

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

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Republic of South Africa National Department of Health



**health**

Department:  
Health  
**REPUBLIC OF SOUTH AFRICA**

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 mother-to-child transmission, please refer to the comprehensive Consolidated HIV Guidelines document and the Guideline for the Prevention of Mother to Child Transmission of Communicable Infections (HIV, Hepatitis, Listeriosis, Malaria, Syphilis and TB) 2019.

### 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.

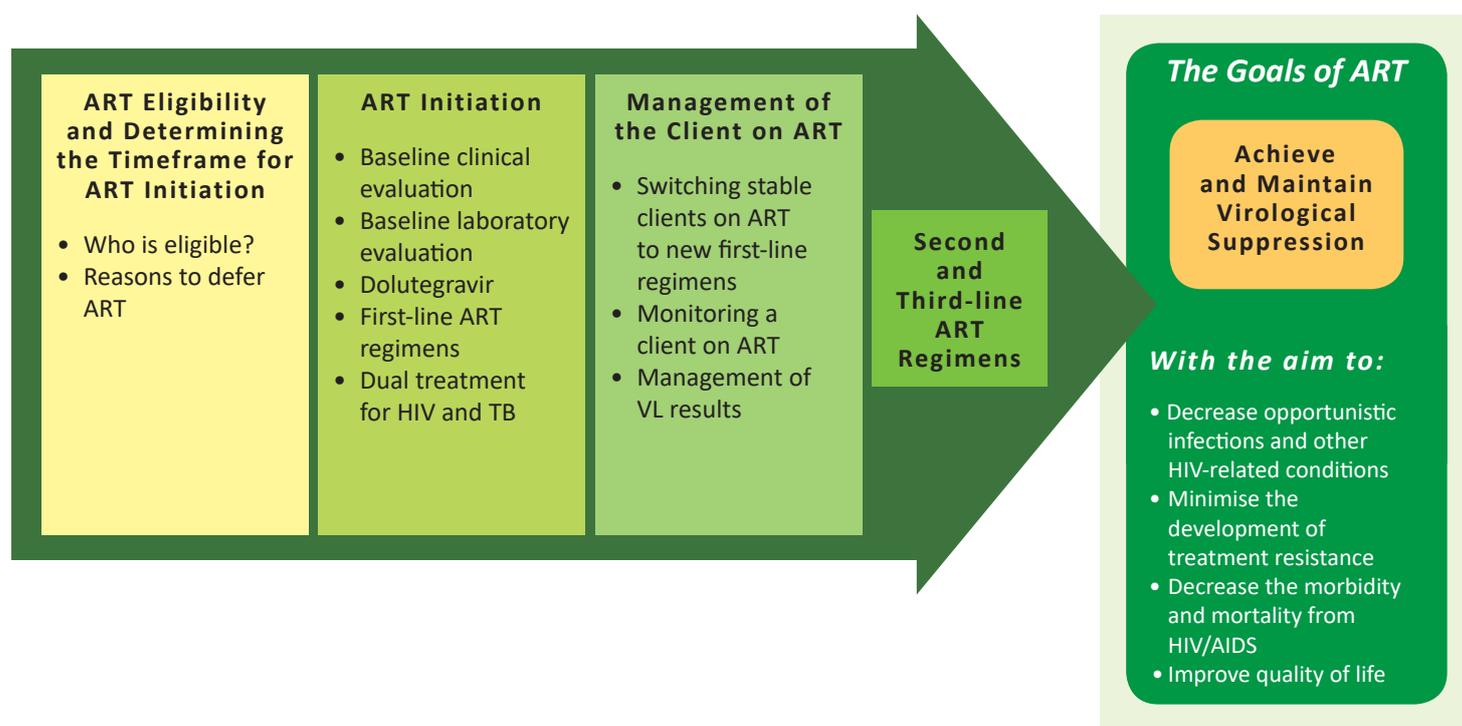
All people either currently on ART, or newly initiated on ART, should be screened for TB and assessed for TB preventive therapy (TPT) as indicated.

The preferred first-line ART regimen is tenofovir disoproxil fumarate-lamivudine-dolutegravir (TLD) for those clients initiating ART, experiencing side-effects to EFV, or for those who prefer to use DTG after being given all the necessary information.

However, due to concerns around safety of TLD in the first trimester of pregnancy, tenofovir disoproxil fumarate-emtricitabine-efavirenz (TEE) is recommended for women of childbearing potential not using contraception and women wanting to conceive. For this reason, integration of family planning and ART services are 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) Second and third-line ART regimens.



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) or drug-resistant (DR) TB at a non-neurological site (e.g. pulmonary TB, abdominal TB, or TB lymphadenitis)	Defer ART initiation as follows: <ul style="list-style-type: none"> <li>• If CD4 &lt; 50 cells/<math>\mu</math>L – initiate ART within 2 weeks of starting TB treatment, when the client's symptoms are improving, and TB treatment is tolerated</li> <li>• If CD4 <math>\geq</math> 50 cells/<math>\mu</math>L – initiate ART 8 weeks after starting TB treatment</li> </ul>
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. <i>Pneumocystis jirovecii</i> 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 $\mu$ mol/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	

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		
		Adults and Adolescents (10-19 years)	Pregnant Women	Children (< 10 years)
<b>Recognise the client</b> with respiratory, neurological, or abdominal <b>danger signs needing urgent care</b>	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
<b>Nutritional Assessment</b>	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 <sup>2</sup> ): < 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
<b>Screen for TB</b>	To identify clients with a positive TB screen who require further investigations for TB 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 <b>TB GeneXpert</b> 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
<b>Screen for symptoms of meningitis</b>	To diagnose and treat clients with cryptococcal and other forms of meningitis and reduce associated morbidity and mortality	<b>Identify symptoms of headache, confusion or visual disturbances.</b> 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 <b>lumbar puncture</b> . 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		
		Adults and Adolescents (10-19 years)	Pregnant Women	Children (< 10 years)
Screen for active depression, other <b>mental health</b> issues or substance abuse	EFV and, to a lesser extent DTG, are associated with neuropsychiatric side-effects. In general, ART can be initiated, and cautiously monitored. Substance use can affect adherence	Screen for symptoms of depression, psychosis, and substance abuse		Screen for symptoms of depression in older children
Screen for major chronic <b>non-communicable diseases (NCDs)</b> (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 <b>pregnancy</b> 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). To assess fertility intentions and contraceptive needs if not pregnant. To assess eligibility for DTG-containing regimens	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 <b>sexually transmitted infections (STIs)</b>	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
<b>Neurodevelopmental screen</b>	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)
<b>WHO clinical stage</b>	<p><b>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:</b></p> <p><b>At ART initiation, WHO clinical stage helps us to:</b>            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 CPT” on page 7)</p>			

**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	Adults and Adolescents (10-19 years)	Pregnant Women	Children (< 10 years)
<b>Confirm HIV test result</b>	To confirm HIV status for those without documented HIV status	✓	✓	✓
<b>CD4 cell count/ %</b>	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
<b>Creatinine and eGFR if TDF used</b>	To assess renal insufficiency	See table titled “Assessing Renal Function” on page 7		N/A
<b>Haemoglobin (Hb)</b>	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 microcytic and manage accordingly <sup>1</sup>	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 <sup>1</sup> Children > 5 years: Do FBC. Characterise according to MCV and manage accordingly <sup>1</sup>
<b>GeneXpert</b>	To diagnose TB	Only for those clients with a <b>positive TB symptom screen</b>	<b>Regardless of TB symptoms</b> , 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 <b>positive TB symptom screen</b>
<b>Cryptococcal antigen test (CrAg) if CD4 &lt; 100 cells/ μL</b>	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 If asymptomatic, provide oral fluconazole If symptomatic, refer for a lumbar puncture	All pregnant women with a positive CrAg should be referred for a lumbar puncture, regardless of symptoms. Fluconazole should be deferred until the second trimester due to teratogenicity concerns, unless there is evidence of active disease	N/A
<b>Cervical cancer screening</b>	To identify women with cervical lesions and manage appropriately	All HIV-positive women should be screened for cervical cancer at diagnosis and subsequently every year if the screening test is negative. If positive, she should be referred for colposcopy and further interventions	Hormonal changes during pregnancy may give false positive or negative results. Delay screening until 6 weeks postpartum	N/A
<b>HBsAg</b>	To identify those co-infected with hepatitis B (HBV)	If positive, exercise caution in stopping TDF-containing regimens, to prevent hepatitis flares		N/A

<sup>1</sup> As outlined in the PHC EML 2018

## Assessing Renal Function

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

<sup>1</sup> Modification of Diet in Renal Disease Study (MDRD) equation

## 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	If CD4 count > 25 % on two tests at least 3-6 months apart
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	If CD4 count > 200 cells/μL on two tests at least 3-6 months apart

## 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)
Pregnant women	Eligible if CD4 count < 100 cells/μL. If CD4 > 100 cells/uL, defer TPT till after delivery*	Isoniazid, oral, 300 mg daily for 12 months and pyridoxine 25 mg daily

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

**Dolutegravir (DTG) Overview**

For further detail on switching **existing stable clients on ART** between regimens, see “Switching Stable Clients on ART Between First-Line Regimens” on page 12

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

**Formulations:**

- Fixed-dose combination: tenofovir (TDF) 300 mg + lamivudine (3TC) 300 mg + DTG 50 mg (TLD). TLD can be prescribed for clients > 35 kg and > 10 years of age
- DTG 50 mg tablet

**Standard Dose:** Children > 20 kg; adolescents and adults: DTG 50 mg daily

**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. Weight gain has emerged as a side effect of this class of drugs; clients who are overweight should receive lifestyle interventions (see below) and obese clients may be considered for EFV. 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 clients’s preference. However, if the client develops insomnia, TLD should be taken in the morning.

**DTG and neural tube defects:** DTG may increase the risk of neural tube defects (NTDs). DTG should be avoided periconception and in the first trimester of pregnancy. DTG appears to be safe if started after the first trimester. The neural tube closes by the end of the fourth week of pregnancy. Thus, there is no risk of NTDs with TLD use after this period. Women of childbearing potential (WOCP) should be counseled regarding the risk of NTDs and advised to use effective contraception if taking DTG.



Care should be provided in ways that respect women’s autonomy in decision-making about their health, and services must provide information and options to **enable women to make informed choices**.<sup>1</sup> Women of childbearing potential should be given all necessary information on DTG- and EFV-containing regimens, including the benefits and potential risks of neural tube defects (NTDs) with DTG use during periconception period, as well as known risks of EFV-based regimens.

Benefits of using DTG	Risks of using DTG	Benefits of using EFV	Risks of using EFV
Provides rapid viral suppression	DTG may increase the risk of neural tube defects (NTDs) if used in the first four weeks after conception	Safe in pregnancy	Low genetic barrier to resistance
High genetic barrier to resistance		No significant interaction with TB treatment	Drug interactions with contraceptives
No interaction with hormonal contraceptives			Neuropsychiatric side-effects
Side-effects are mild and uncommon			

**FEMALE CONTRACEPTIVE METHODS**



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.

<sup>1</sup> "Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV July 2018", page 5. Available at: <http://apps.who.int/iris/bitstream/handle/10665/273632/WHO-CDS-HIV-18.18-eng.pdf?ua=1>

## Lifestyle Interventions

All clients should be encouraged to apply the following lifestyle changes as appropriate: Maintain an ideal weight, i.e. BMI < 25 kg/m<sup>2</sup>. Overweight clients with BMIs > 25 kg/m<sup>2</sup> should reduce their weight. Alcohol intake should be reduced to < 2 standard drinks per day for men, and < 1 for women on no more than 5 out of 7 days per week. A prudent eating plan should be followed i.e. low fat, high fibre and unrefined carbohydrates, with fresh fruit and vegetables. Regular moderate aerobic exercise, e.g. 30 minutes of brisk walking 3-5 times per week (150 minutes/week). The client should be advised to stop smoking.

## Drug Interactions with Dolutegravir

Interacting Drug	Effect of Co-Administration	Recommendation
Rifampicin	 Dolutegravir	Double DTG dose to 50 mg 12-hourly. If on TLD FDC, add DTG 50 mg 12 hours after TLD dose
Polyvalent cations (Mg <sup>2+</sup> , Fe <sup>2+</sup> , Ca <sup>2+</sup> , Al <sup>3+</sup> , Zn <sup>2+</sup> ) e.g. antacids, sucralfate, multivitamin and nutritional supplements	 Dolutegravir	Take DTG either 2 hours before or 6 hours after a medicine or food supplement containing a polyvalent cation
Anticonvulsants: • Carbamazepine • Phenobarbital • Phenytoin • Valproate	 Dolutegravir	Avoid coadministration if possible (lamotrigine, levetiracetam, and topiramate do not interact with DTG, and can be used). Double DTG dose to 50 mg 12-hourly for carbamazepine if alternative anticonvulsant cannot be used
Metformin	 Metformin	Maximum metformin dose 500 mg 12-hourly

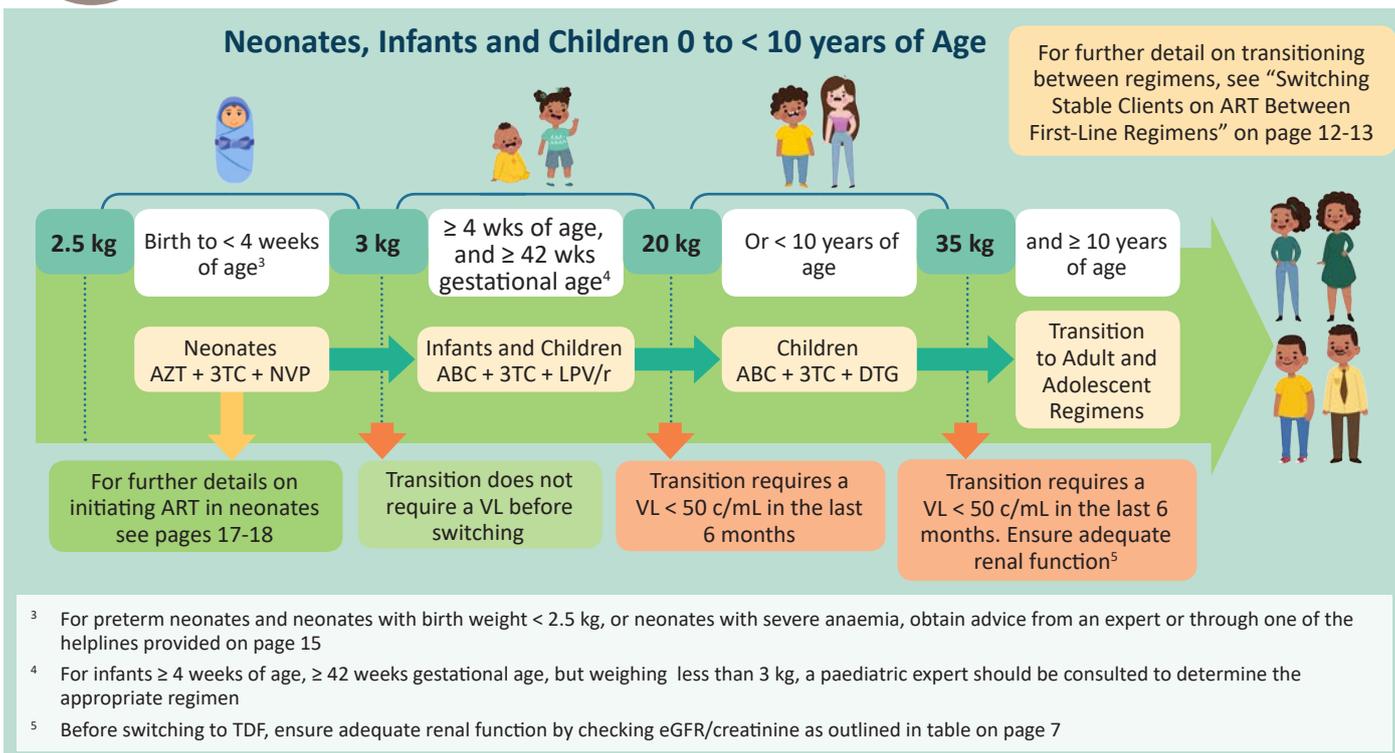
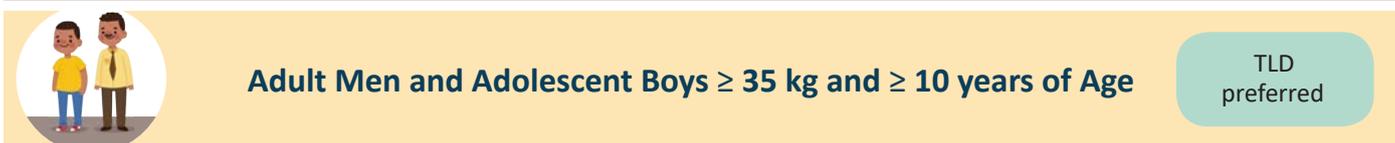
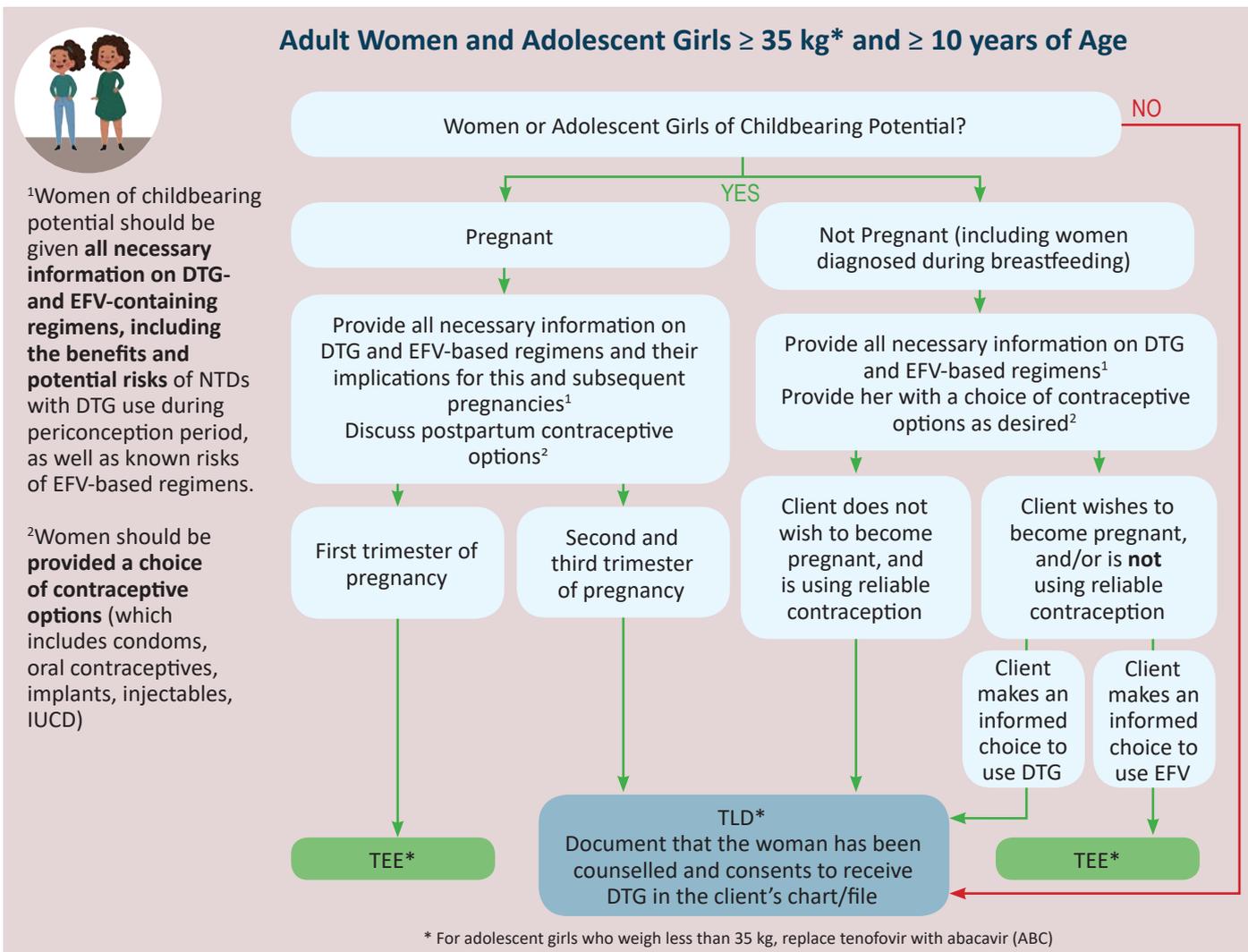
Drug interactions can result in suboptimal drug levels which can cause

- an elevated viral load
- drug resistance, due to replicating virus in the presence of subtherapeutic drug levels



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](http://www.hiv-druginteractions.org/checker),  
the Liverpool HIV iChart application for smart phones,  
or any of the helplines provided on page 15





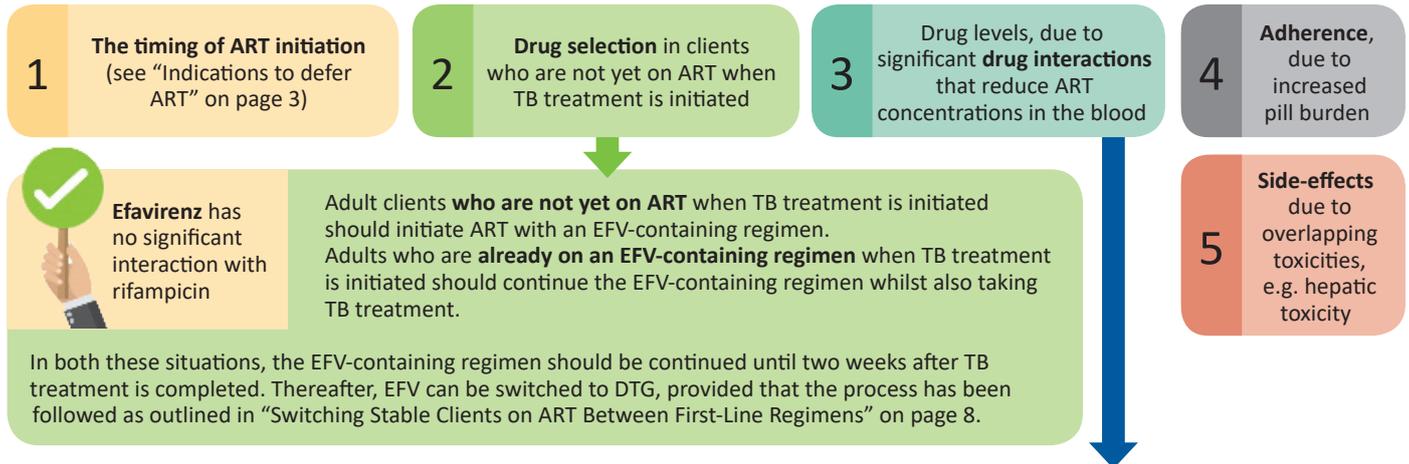
## ART Initiation in Women and Adolescent Girls Diagnosed with HIV during Labour

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 after appropriate counselling to understand her fertility intentions and contraceptive needs:

TLD can be provided if she: 1) does not wish to become pregnant, 2) is willing to use contraception, or 3) has been given all necessary information on DTG-containing regimens and has made an informed decision to use TLD. If not, start TEE. Appropriate ART literacy education should be given to the woman before she leaves the facility. Provide a **2-month supply** of first-line ART regimen at discharge from labour ward.

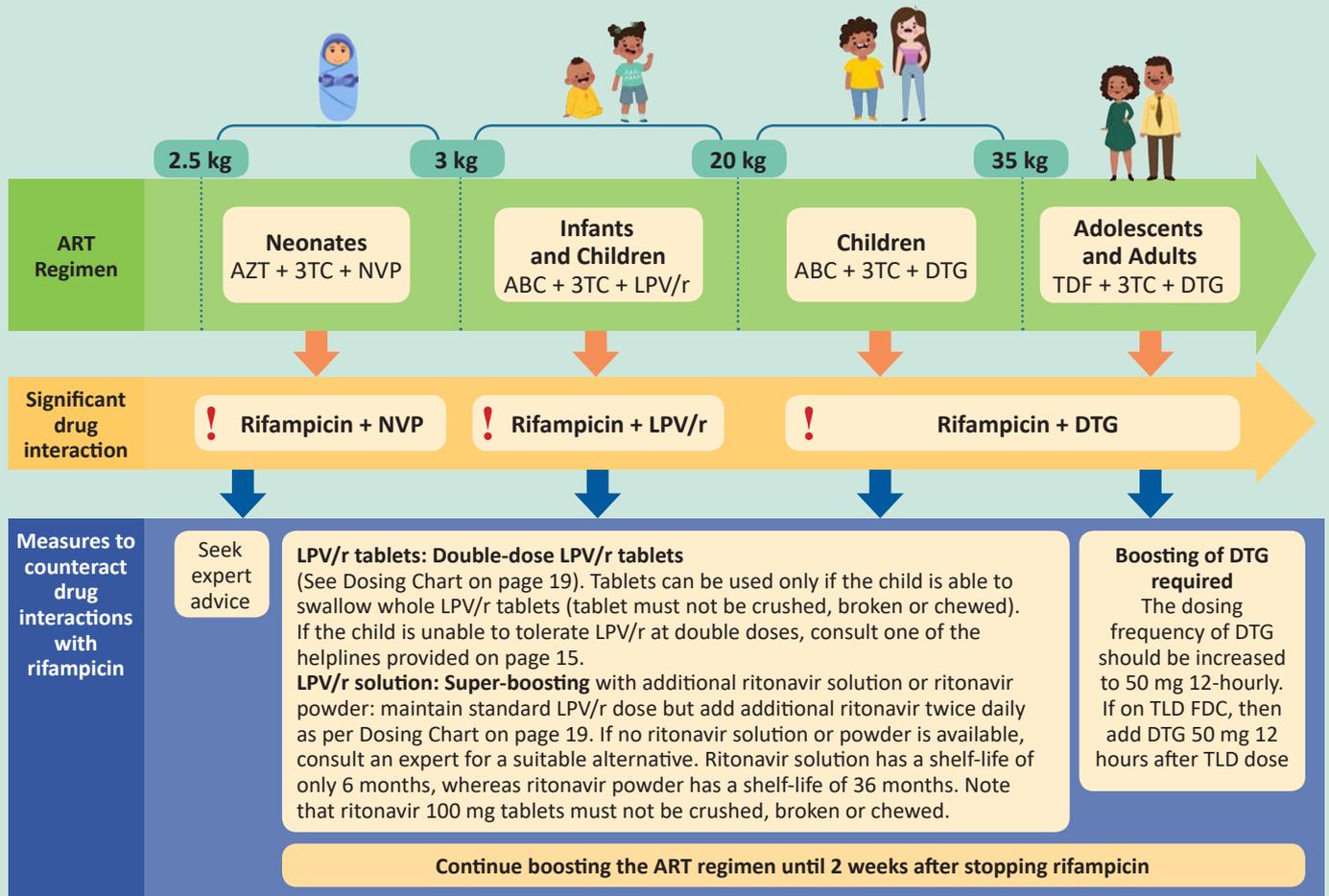
## Dual Treatment of HIV and Active TB in Neonates, Infants, Children, Adolescents and Adults

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



### Drug Interactions

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





## Managing the Client on ART

### Switching Stable Clients on ART Between First-Line Regimens



#### Switching Adults, and Adolescents who are on First-line Adult Regimens

##### Routine VL Monitoring:

(First VL at 6 months on ART. If virally suppressed (< 50 c/mL), repeat VL at 12 months on ART, and 12-monthly thereafter if viral load remains suppressed)

Check if client has a VL result in the last 6 months\*

VL < 50 c/mL

VL 50 - 1000 c/mL

VL > 1000 c/mL

Provide enhanced adherence support  
Repeat VL in 3 months

VL 50 - 1000 c/mL

Ensure that the elevated VL is correctly managed according to the **VL results management algorithm** on page 15  
Do not switch to DTG at this time

Provide information on the risks and benefits of DTG, and the use of contraception in WOCBP (see page 8). Enable the client to make an informed decision.

Client chooses to remain on their current regimen

Client chooses to switch to DTG

If current regimen is  
TDF + 3TC/FTC + EFV/NVP

If current regimen is  
AZT/ABC<sup>2</sup> + 3TC + EFV/NVP

Switch to TDF + 3TC/FTC + DTG<sup>1</sup>

Switch to AZT/ABC + 3TC + DTG<sup>1</sup>



Only switch a **stable pregnant woman** on ART from EFV to DTG if her VL is < 50 copies/mL, and she is **no longer in the first trimester**. A switch to DTG needs to be preceded by WOCBP being given all necessary information on DTG-containing regimens, provision of postpartum contraceptive options if desired, and information on the new side-effects that may be experienced when switching to a new drug.



Warn the client of the new side-effects that may be experienced when switching to DTG (insomnia, headache, GIT disturbances). These are usually mild and self-limiting. If the client experiences insomnia, DTG can be taken in the morning.



\*If a client has not had a VL test in the last 6 months, additional VL testing outside of the routine VL monitoring schedule should NOT be done. The client should await the result of their routine annual VL test to determine their eligibility to switch to DTG.

<sup>1</sup> Discuss and provide sexual and reproductive health services for the sexually active adolescent/adult.

<sup>2</sup> Assess the reason for exclusion of TDF from the NRTI backbone. If TDF was excluded due to TDF-induced nephrotoxicity, continue using the same NRTI backbone. If TDF was excluded due to non-TDF related renal failure that has since resolved, the use of TDF can be reconsidered. Before switching to TDF, ensure adequate renal function by checking eGFR/creatinine as outlined in the table "Assessing Renal Function" on page 7



## Switching Children and Adolescents who are on First-Line Paediatric Regimens

Children and adolescents currently on the following first-line regimens and weighing > 20 kg:

ABC + 3TC + LPV/r<sup>1</sup>

or

ABC + 3TC + EFV

### Routine VL Monitoring:

(First VL at 6 months on ART. If virally suppressed (< 50 c/mL), repeat VL at 12 months on ART, and 12-monthly thereafter if viral load remains suppressed)

Check if client has a VL result in the last 6 months\*

VL < 50 c/mL

VL 50 - 1000 c/mL

VL > 1000 c/mL

Provide enhanced adherence support  
Repeat VL in 3 months

Ensure that the elevated VL is correctly managed according to the **VL results management algorithm** on page 15  
Do not switch to DTG at this time

VL 50 - 1000 c/mL

Provide information on the risks and benefits of DTG, and the implications for childbearing in later years (see "Dolutegravir" on page 8). Enable the caregiver/adolescent to make an informed decision

Client chooses to remain on their current regimen

Caregiver/adolescent chooses to switch to DTG

Weight > 20 kg and < 35 kg, or < 10 years of age

Weight ≥ 35 kg and age ≥ 10 years, and renal function normal<sup>3</sup>

ABC + 3TC + DTG<sup>2</sup>

Renal function abnormal

If weight reaches 35 kg or more, and VL < 50 c/mL in the last 6 months, and renal function is normal<sup>3</sup>

TDF<sup>3</sup> + 3TC + DTG<sup>2</sup>

**!** \*If a client has not had a VL test in the last 6 months, additional VL testing outside of the routine VL monitoring schedule should NOT be done. The client should await the result of their routine annual VL test to determine their eligibility to switch to DTG.

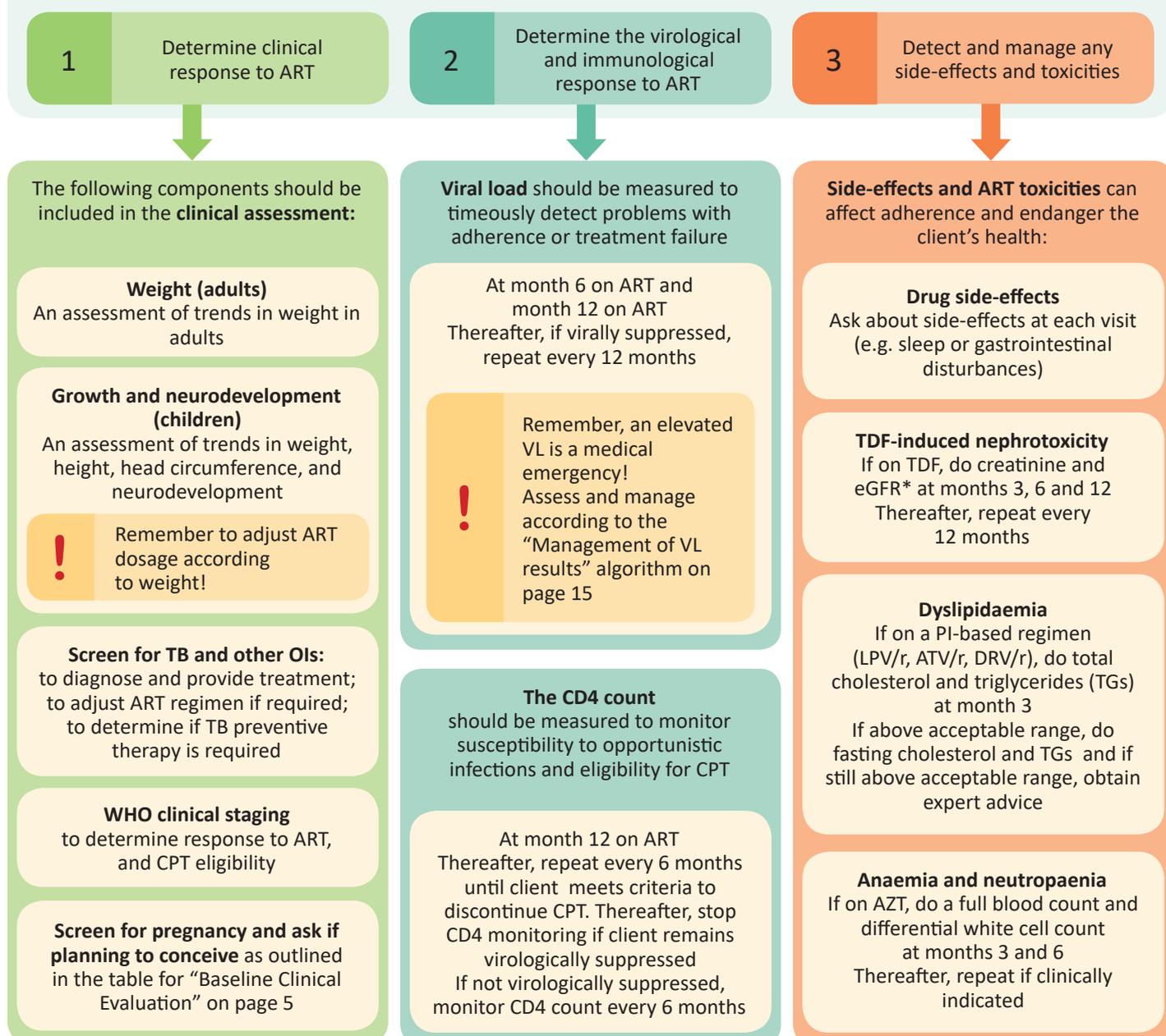
<sup>1</sup> Switching LPV/r to DTG in this regimen applies strictly to first-line regimens only. If ABC + 3TC + LPV/r is used as a second-line regimen, it is possible that both NRTIs in the regimen are inactive. DTG should not be used without at least 1 active NRTI. If DTG is to be considered within a second-line regimen, expert guidance should be sought to ensure that at least 1 NRTI is active.

<sup>2</sup> Discuss and provide sexual and reproductive health services for the sexually active adolescent/adult.

<sup>3</sup> Before switching to TDF, ensure adequate renal function by checking eGFR/creatinine as outlined in the table "Assessing Renal Function" on page 7

## 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:

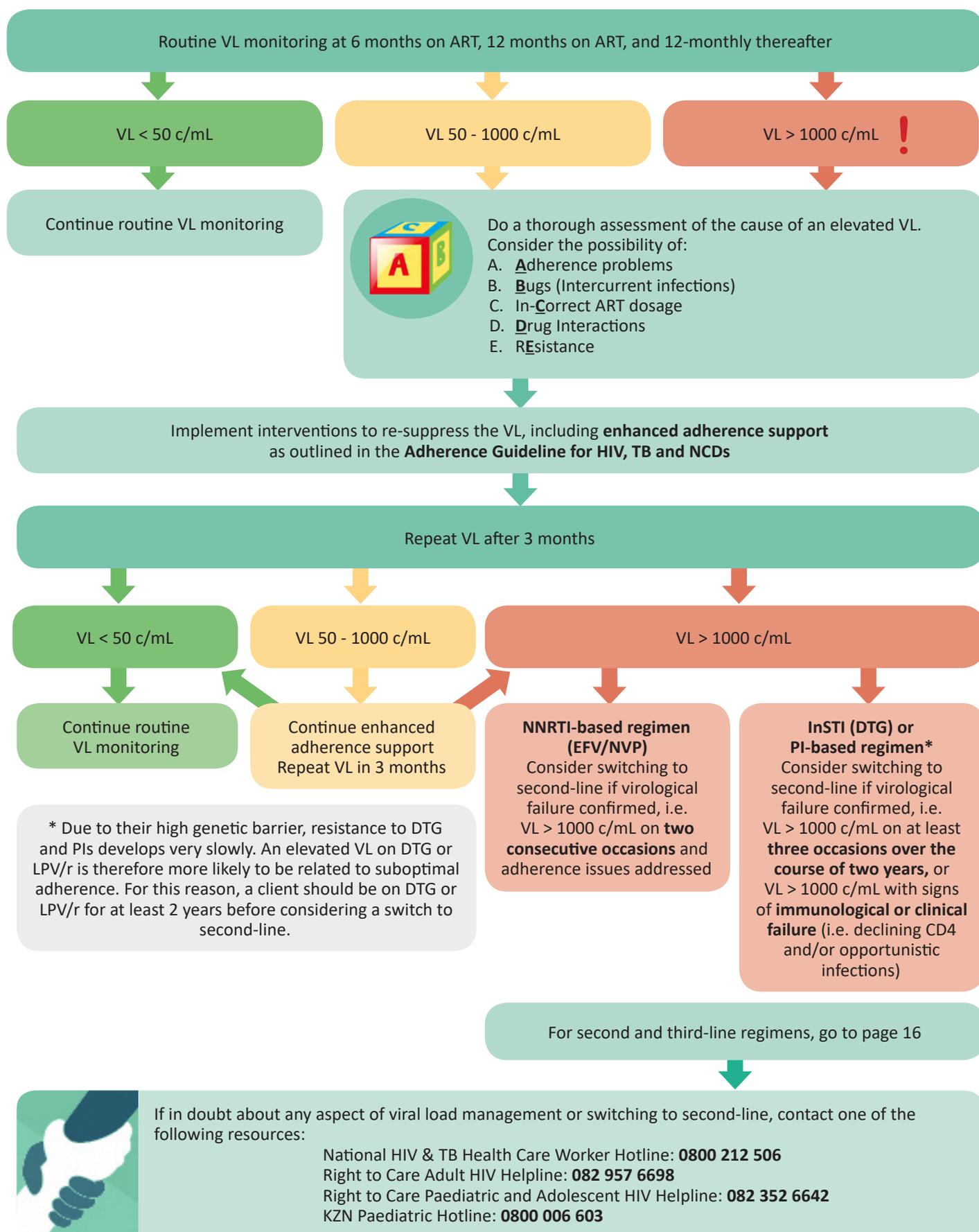


### \*Assessing Renal Function

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

<sup>1</sup> Modification of Diet in Renal Disease Study (MDRD) equation

## Management of Viral Load Results in Infants, Children, Adolescents and Adults



## Second-Line (2L) and Third-Line (3L) ART Regimens

If in doubt about any aspect of switching to second-line, contact one of the helplines provided on page 15

### Second-line ART Regimens for Adults with Confirmed Virological Failure



	First-Line Regimens				Second-Line Regimens	
	NNRTI-based Regimen		InSTI-based Regimen for > 2 years		PI-based Regimen for > 2 years	
Regimen	TDF + 3TC/FTC + EFV/NVP		TDF + 3TC/FTC + DTG		AZT/TDF + 3TC/FTC + LPV/r or ATV/r	
Resistance Testing	Resistance test <u>not</u> required		Resistance testing may be required under expert consultation <sup>5</sup>		Resistance test required	
Resistance Test results	Not applicable		Not applicable		No PI resistance	PI resistance
HBV Co-infection Status <sup>1</sup>	HBV-negative	HBV-positive	HBV-negative	HBV-positive	HBV-positive or -negative	
New Regimen	AZT + 3TC/FTC + DTG <sup>2</sup>	TDF <sup>1</sup> + AZT + 3TC/FTC + DTG <sup>2</sup>	AZT + 3TC/FTC + LPV/r	TDF + 3TC/FTC + LPV/r <sup>4</sup>	Continue current regimen and address adherence	Refer to Third-Line Committee. Regimen will be determined by results of resistance test
	If DTG not suitable, AZT + 3TC/FTC + LPV/r	If DTG not suitable, TDF + 3TC + LPV/r <sup>4</sup>				

### Second and Third-line ART Regimens for Children and Adolescents with Confirmed Virological Failure



All children and adolescents with confirmed virological failure should be discussed with an expert.

	NNRTI-based Regimen		PI-based Regimen for > 2 years			InSTI-based Regimen for > 2 years	
	Regimen	ABC/AZT/TDF + 3TC/FTC + EFV/NVP		ABC/AZT/TDF + 3TC/FTC + LPV/r or ATV/r			ABC/AZT/TDF + 3TC/FTC + DTG
Resistance Testing	Resistance test not required		Resistance test required			Resistance test required	
Resistance Test Results	Not applicable		No PI resistance		PI resistance (or genotype unsuccessful)	No InSTI resistance	InSTI resistance
Weight	< 20 kg	≥ 20 kg	< 20 kg	≥ 20 kg	All	All children/adolescents on DTG will be ≥ 20 kg	
New Regimen or Other Action Required	ABC/AZT + 3TC + LPV/r <sup>4</sup>	2 NRTIs + DTG <sup>2</sup> In consultation with an expert, ensure that at least 1 NRTI is active <sup>3</sup>	Continue current regimen and address adherence	2 NRTIs + DTG <sup>2</sup> In consultation with an expert, ensure that at least 1 NRTI is active <sup>3</sup>	Refer to Third-line committee	2 NRTIs + DTG <sup>2</sup> In consultation with an expert, ensure that at least 1 NRTI is active <sup>3</sup>	Refer to Third-line committee
		If NRTI activity cannot be confirmed, expert will recommend 2 NRTIs + PI/r		If NRTI activity cannot be confirmed, expert will recommend 2 NRTIs + PI/r. Adherence must be addressed		If NRTI activity cannot be confirmed, refer to Third-line committee	

<sup>1</sup> Always check hepatitis B status before stopping TDF. If client has chronic hepatitis B, stopping TDF may lead to a severe hepatitis flare. If hepatitis B-positive, TDF should be continued in the second-line regimen.

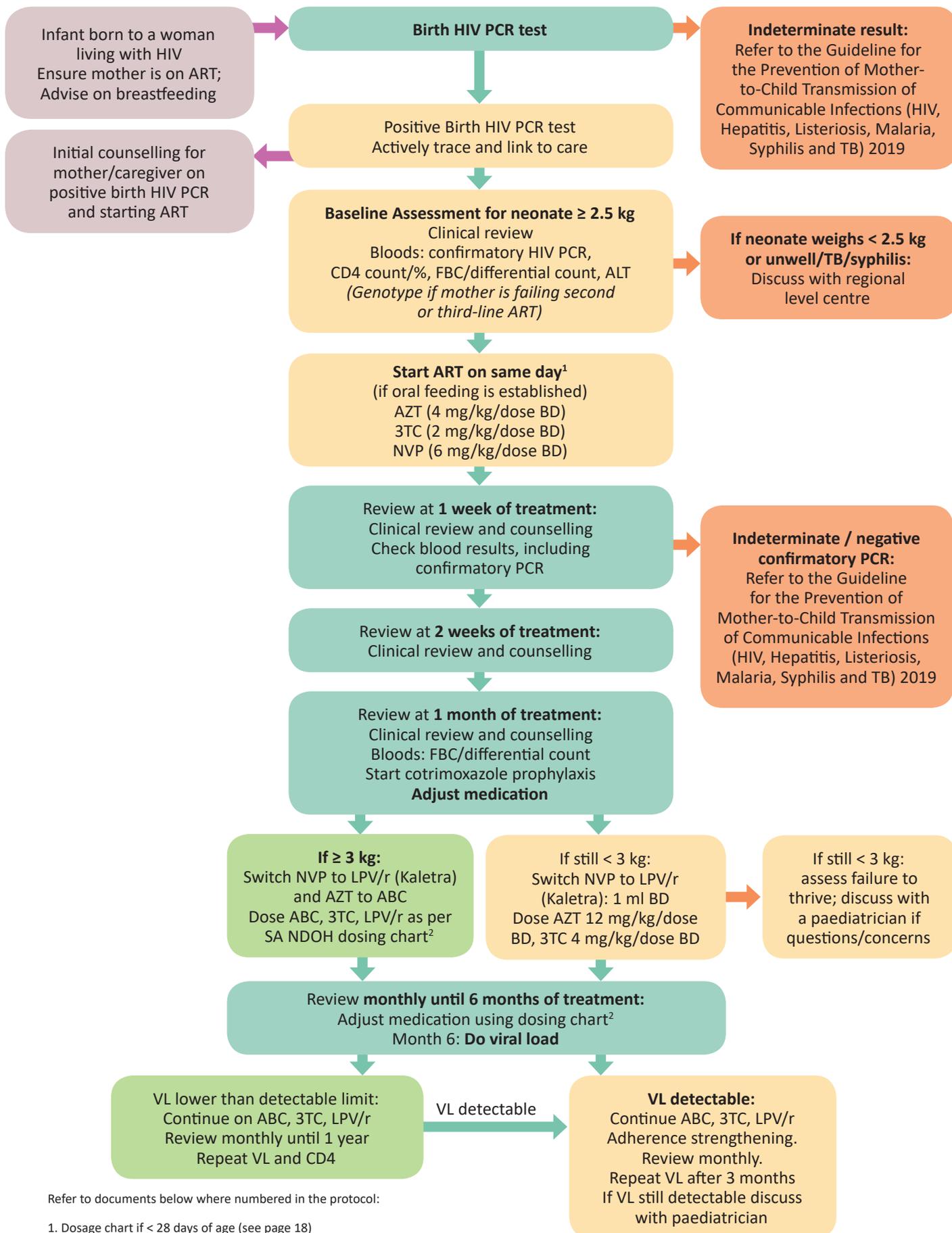
<sup>2</sup> Prior to DTG initiation, all women and adolescent girls of childbearing potential must be appropriately counseled on the potential risk of NTDs with DTG use around conception time and provided with contraceptives as desired (see "Dolutegravir" on page 8).

<sup>3</sup> From the DAWNING study, DTG was shown to achieve viral suppression when used with at least one NRTI that is known to have genotypic resistance (Aboud M et al., IAS Oral abstract, 2017). It is yet unknown if DTG will work if combined with two inactive NRTIs.

<sup>4</sup> In the EARNEST study, LPV/r was shown to be effective even if combined with two NRTIs that are known to have genotypic resistance (Paton, et al., N Engl J Med, 2014). For this reason, AZT is omitted from LPV/r-containing regimens when TDF is continued due to HBV co-infection. Resistant NRTIs may be recycled with an active PI if no other feasible options are available.

<sup>5</sup> Resistance testing in clients failing DTG may be authorised by an expert on a case-by-case basis.

**Protocol for initiation of ART in HIV-infected neonates  $\geq 2.5$  kg at birth**



Refer to documents below where numbered in the protocol:

- 1. Dosage chart if < 28 days of age (see page 18)
- 2. SA NDOH dosing chart (see page 19)

Please note, this protocol is meant as a guide, and there is allowance for flexibility after discussion with an expert.



## ARV Drug Dosing Chart for Children from birth - 28 days of age with birth weight $\geq 2.5$ kg ( $\geq 35$ weeks gestational age at birth)

	Lamivudine (3TC)		Zidovudine (AZT)		Nevirapine (NVP)	
Target dose	2 mg/kg/dose TWICE daily (BD)		4 mg/kg/dose TWICE daily (BD)		6 mg/kg/dose TWICE daily (BD)	
Available formulation	10 mg/mL		10 mg/mL		10 mg/mL	
Weight (kg)	Dose in mL	Dose in mg	Dose in mL	Dose in mg	Dose in mL	Dose in mg
$\geq 2.5$ - $< 3$	0.5 mL BD	5 mg BD	1 mL BD	10 mg BD	1.5 mL BD	15 mg BD
$\geq 3$ - $< 4$	0.8 mL BD	8 mg BD	1.5 mL BD	15 mg BD	2 mL BD	20 mg BD
$\geq 4$ - $< 5$	1 mL BD	10 mg BD	2 mL BD	20 mg BD	3 mL BD	30 mg BD

- Dosing is based on the birth weight of the child and it is not necessary to change the dose before 28 days of age (for example if the weight decreases in the first week or two of life)
- Caregivers who will be administering ARV medication to the child must be supplied with a syringe (2 mL or 5 mL) for each of the 3 ARVs and shown how to prepare and administer the correct dose. If required, bottles and syringes should be colour coded with stickers and a sticker of the relevant colour used to mark the correct dose on the syringe.

Adapted from: Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV: interim guidelines. Supplement to the 2016 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2018



# Antiretroviral Drug Dosing Chart for Children (2019)

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

Target dose	Abacavir (ABC)	Lamivudine (3TC)	Zidovudine (AZT)	Lopinavir / ritonavir (LPV/r)	Lopinavir/ritonavir when on rifampicin (and for 2 weeks after stopping rifampicin) Choose one of the 3 options below as appropriate	"Atazanavir (ATV) + ritonavir (RTV)	Dolutegravir (DTG)	Dolutegravir when on rifampicin	Efavirenz (EFV)	Target dose								
8 mg/kg/dose TWICE daily OR 16 mg/kg/dose ONCE daily	4 mg/kg/dose TWICE daily OR 8 mg/kg/dose ONCE daily	180-240 mg/m <sup>2</sup> /dose TWICE daily	300/75 mg/m <sup>2</sup> /dose TWICE daily	LPV/r std dose + super-boosting with ritonavir (RTV) solution TWICE daily (≥ 0.75 x LPV dose bd)	LPV/r std dose + super-boosting with ritonavir (RTV) powder TWICE daily (≥ 0.75 x LPV dose bd)	ATV caps 150, 200 mg; RTV tabs 100 mg	By weight band ONCE daily	By weight band TWICE daily	By weight band ONCE daily	Target dose								
Sol. 20 mg/ml Tabs 60 mg (scored, dispersible), 300 mg (not scored). FDC: ABC/3TC 600/300 mg	Sol. 10 mg/ml Tabs 150 mg (scored), FDC: ABC/3TC 600/300 mg	Sol. 10 mg/ml Tabs 100 mg, 300 mg (not scored). FDC: AZT/3TC 300/150 mg	Sol. 80/20 mg/ml Adult tabs 200/50 mg, Paeds tabs 100/25 mg <b>TABLETS MUST BE SWALLOWED WHOLE</b>	Solution 80 mg/ml	Adult tabs 200/50 mg, Paed tabs 100/25 mg	ATV caps 150, 200 mg; RTV tabs 100 mg	By weight band ONCE daily	By weight band TWICE daily	Caps/tabs 50, 200, 600 mg (not scored); FDC: TEE 300/200/600 mg	Available formulations								
2 ml bd OR 3 ml bd OR 4 ml bd	2 ml bd OR 3 ml bd OR 4 ml bd	6 ml bd OR 9 ml bd OR 12 ml bd OR 1 x 100 mg tab bd	*1 ml bd OR *1.5 ml bd OR 2 ml bd OR 2 x 100/25 mg paed tabs am + 1 x 100/25 mg paed tab pm OR Choose only one option: 2.5 ml bd OR 2 x 100/25 mg paed tabs bd OR 1 x 200/50 mg adult tab bd OR Choose only one option: 3 ml bd OR 2 x 100/25 mg paed tabs bd OR 1 x 200/50 mg adult tab bd OR Choose only one option: 3.5 ml bd OR 3 x 100/25 mg paed tabs bd OR + 1 x 200/50 mg adult tab bd OR 1 x 100/25 mg paed tab bd OR Choose only one option: 5 ml bd OR 4 x 100/25 mg paed tabs bd OR - 2 x 200/50 mg adult tabs bd	1 ml bd OR 1.5 ml bd OR 1.5 ml bd OR 2 ml bd OR 2.5 ml bd OR 3 ml bd OR 4 ml bd	Do not use double-dose LPV/r tabs OR 3 x 100/25 mg tabs bd OR 4 x 100/25 mg tabs bd OR 2 x 200/50 mg tabs bd OR 6 x 100/25 mg tabs bd OR 3 x 200/50 mg tabs bd OR 4 x 200/50 mg tabs bd OR 8 x 100/25 mg tabs bd	Avoid ATV capsules when < 15 kg or < 6 years OR ATV 1 x 200 mg cap od + RTV 1 x 100 mg tab od	Not currently recommended: dosing and formulations not available OR 1 x 50 mg tab od OR 1 x 50 mg tab bd	Not currently recommended: dosing and formulations not available OR 1 x 200 mg cap/tab + 2 x 50 mg caps/tabs nocte OR 2 x 200 mg caps/tabs nocte	Wt. (kg)									
10-10.9	11-13.9	14-14.9	15-16.9	17-19.9	20-22.9	23-24.9	25-29.9	30-34.9	35-39.9	≥ 40								
< 3	3-3.9	4-4.9	5-5.9	6-6.9	7-7.9	8-8.9	9-9.9	10-10.9	11-13.9	14-14.9	15-16.9	17-19.9	20-22.9	23-24.9	25-29.9	30-34.9	35-39.9	≥ 40

Currently available tablet formulations of abacavir (except 60 mg), zidovudine, lamivudine, lopinavir/ritonavir, ritonavir, dolutegravir & efavirenz must be swallowed whole and NOT chewed, divided or crushed

Consult with a clinician experienced in paediatric ARV prescribing for neonates (< 28 days of age) and infants weighing < 3kg

\* Avoid LPV/r solution in any full-term infant < 14 days of age and any premature infant < 42 weeks postconceptional 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  
 Abbreviations: od, once a day; nocte, at night; bd, twice a day; am, in the morning; pm, in the evening; std, standard; FDC, fixed dose combination; TLD, tenofovir/lamivudine/dolutegravir; TEE, tenofovir/emtricitabine/efavirenz

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



## Other Resources and Important Information

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### **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](mailto: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](mailto: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](mailto:pha-mic@uct.ac.za)

SMS/please call me/WhatsApp (071) 840-1572

**Right to Care Paediatric and Adolescent HIV Helpline** (082) 352-6642

**Right to Care Adult HIV Helpline** (082) 957-6698

Both Right to Care Helplines can be contacted via call/ SMS/please call me/WhatsApp

**KZN Paediatric Hotline:** 0800 006 603

#### **Disclaimer:**

The information presented in these guidelines conforms to the current medical, nursing and pharmaceutical practice.

Contributors and editors cannot be held responsible for errors, individual responses to medicines, and other consequences.



## Abbreviations

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3TC	Lamivudine
ABC	Abacavir
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
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
DTG	Dolutegravir
eGFR	Estimated glomerular filtration rate
EFV	Efavirenz
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
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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