2019 ART Clinical Guidelines
for the Management of HIV in Adults, Pregnancy, Adolescents, Children, Infants and Neonates

Published: October 2019
Republic of South Africa National Department of Health
# Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreword</td>
<td>1</td>
</tr>
<tr>
<td>Overview</td>
<td>2</td>
</tr>
<tr>
<td>The Goals of ART</td>
<td>2</td>
</tr>
<tr>
<td>ART Eligibility</td>
<td>3</td>
</tr>
<tr>
<td>Medical Indications to Defer ART</td>
<td>3</td>
</tr>
<tr>
<td>ART Initiation</td>
<td>4</td>
</tr>
<tr>
<td>Baseline Clinical Evaluation for Adults and Adolescents, Pregnant Women, and Children &lt; 10 years</td>
<td>4</td>
</tr>
<tr>
<td>Baseline Laboratory Evaluation for Adults and Adolescents, Pregnant Women, and Children</td>
<td>6</td>
</tr>
<tr>
<td>Indications for Starting and Stopping Cotrimoxazole Preventive Therapy (CPT)</td>
<td>7</td>
</tr>
<tr>
<td>TB Preventive Therapy</td>
<td>7</td>
</tr>
<tr>
<td>Dolutegravir</td>
<td>8</td>
</tr>
<tr>
<td>First-Line ART Regimens in Adults, Adolescents, Pregnant Women, Children, Infants, and Neonates</td>
<td>10</td>
</tr>
<tr>
<td>Re-initiating ART in Clients who have Interrupted Treatment</td>
<td>11</td>
</tr>
<tr>
<td>Dual Treatment of HIV and Active TB in Neonates, Infants, Children, Adolescents and Adults</td>
<td>12</td>
</tr>
<tr>
<td>Managing the Client on ART</td>
<td>13</td>
</tr>
<tr>
<td>Switching Stable Clients on ART Between First-Line Regimens</td>
<td>13</td>
</tr>
<tr>
<td>Monitoring on ART</td>
<td>15</td>
</tr>
<tr>
<td>Management of Viral Load Results in Infants, Children, Adolescents and Adults</td>
<td>16</td>
</tr>
<tr>
<td>Second-Line (2L) and Third-Line (3L) ART Regimens</td>
<td>17</td>
</tr>
<tr>
<td>Second-line ART Regimens for Adults with Confirmed Virological Failure</td>
<td>17</td>
</tr>
<tr>
<td>Second and Third-line ART Regimens for Children and Adolescents with Confirmed Virological Failure</td>
<td>17</td>
</tr>
<tr>
<td>Annexures</td>
<td>18</td>
</tr>
<tr>
<td>Protocol for initiation of ART in HIV-infected neonates ≥ 2.5 kg at birth</td>
<td>18</td>
</tr>
<tr>
<td>ARV Drug Dosing Chart for Children from birth - 28 days of age with birth weight ≥ 2.5 kg</td>
<td>19</td>
</tr>
<tr>
<td>Antiretroviral Drug Dosing Chart for Children (2019)</td>
<td>20</td>
</tr>
<tr>
<td>Other Resources and Important Information</td>
<td>22</td>
</tr>
<tr>
<td>Abbreviations</td>
<td>23</td>
</tr>
</tbody>
</table>
Foreword

South Africa is committed to attaining the UNAIDS 90-90-90 targets to control the HIV epidemic through quality comprehensive health services and use of highly effective antiretroviral treatment (ART). The principal goal of ART is to attain and maintain viral suppression, which will decrease morbidity and mortality from HIV as well as improve the quality of life for clients living with HIV.

The 2019 HIV clinical guidelines have been revised to include a new formulation of the fixed dose combination (FDC) of Tenofovir (TDF) 300 mg + Lamivudine (3TC) 300 mg + Dolutegravir (DTG) 50 mg (TLD) for all eligible adults, adolescents and children over the age of 10 years and weighing 35 kg or more. This document intends to serve as a quick reference guide and job aid for healthcare workers. It intends to:

- Provide guidance on initiating naïve clients on DTG-containing regimens
- Provide guidance on switching existing clients on ART to DTG-containing regimens
- Highlight critical areas for the provision of integrated ART, TB and family planning services
- Provide guidance on second and third line regimens in the era of DTG.

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

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

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

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

Dr Anban Pillay
Acting Director General: Health
Overview

This ART Clinical Guideline is intended to serve as a quick reference guide for antiretroviral treatment (ART) in adults, pregnant women, adolescents and paediatric clients, and as a job aide for healthcare workers and implementing partners. This document is not intended to be exhaustive; for more information or details on any recommendations, or on the prevention of 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 first 6 weeks of pregnancy, tenofovir disoproxil fumarate-emtricitabine-efavirenz (TEE) is recommended for women of childbearing potential 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.

The Goals of ART

Achieve and Maintain Virological Suppression

With the aim to:

- Decrease opportunistic infections and other HIV-related conditions
- Minimise the development of treatment resistance
- Decrease the morbidity and mortality from HIV/AIDS
- Improve quality of life

ART Eligibility and Determining the Timeframe for ART Initiation

- Who is eligible?
- Reasons to defer ART

ART Initiation

- Baseline clinical evaluation
- Baseline laboratory evaluation
- Dolutegravir
- First-line ART regimens
- Dual treatment for HIV and TB

Management of the Client on ART

- Switching stable clients on ART to new first-line regimens
- Monitoring a client on ART
- Management of VL results

Second and Third-line ART Regimens
ART Eligibility

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

Medical Indications to Defer ART

<table>
<thead>
<tr>
<th>Indication</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB symptoms (cough, night sweats, fever, recent weight loss)</td>
<td>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.</td>
</tr>
</tbody>
</table>
| 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 |
| Diagnosis of drug-resistant (DR) TB at a non-neurological site (e.g. pulmonary TB, abdominal TB, or TB lymphadenitis) | Initiate ART after 2 weeks of TB treatment, when the client’s symptoms are improving, and TB treatment is tolerated |
| Diagnosis of DS-TB or DR-TB at a neurological site (e.g. TB meningitis or tuberculoma) | Defer ART until 4-8 weeks after start of TB treatment |
| Signs and symptoms of meningitis | Investigate for meningitis before starting ART |
| Cryptococcal antigen (CrAg) positive in the absence of symptoms or signs of meningitis | Defer ART until the first 2 weeks of fluconazole prophylaxis has been completed |
| Confirmed cryptococcal meningitis | Defer ART until 4-6 weeks of antifungal treatment has been completed |
| Other acute illnesses e.g. *Pneumocystis jirovecii* pneumonia (PJP) or bacterial pneumonia | Defer ART for 1-2 weeks after commencing treatment for the infection |
| Clinical symptoms or signs of liver disease | Confirm liver injury using ALT and total bilirubin levels. ALT elevations > 120 IU/L with symptoms of hepatitis, and/or total serum bilirubin concentrations > 40 µmol/L are significant. Investigate and manage possible causes including hepatitis B, drug-induced liver injury (DILI), or alcohol abuse |

Note: Clients who are already on ART should NOT have their treatment interrupted upon diagnosis of the above conditions.
ART Initiation

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

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

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

<table>
<thead>
<tr>
<th>Component of the Baseline Clinical Evaluation</th>
<th>Purpose</th>
<th>Further Action Required</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recognise the client</strong>&lt;br&gt;with respiratory, neurological, or abdominal danger signs needing urgent care</td>
<td>To identify opportunistic infections and conditions needing urgent care or referral</td>
<td>Identify respiratory, neurological, or abdominal danger signs as outlined in Adult Primary Care (APC) guideline</td>
</tr>
<tr>
<td><strong>Nutritional Assessment</strong></td>
<td>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</td>
<td>Measure weight and height and determine BMI (kg/m²): &lt; 18.5 = underweight; 18.5 to 25 = normal; &gt; 25 to &lt; 30 = overweight; ≥30 = obese</td>
</tr>
<tr>
<td><strong>Screen for TB</strong></td>
<td>To identify clients with a positive TB screen who require further investigations for TB&lt;br&gt;<strong>To identify clients with a negative TB screen who may be eligible for TPT</strong> (see page 7)</td>
<td>Identify symptoms of cough, night sweats, fever, recent weight loss as outlined in the TB screening tool</td>
</tr>
<tr>
<td><strong>Screen for symptoms of meningitis</strong></td>
<td>To diagnose and treat clients with cryptococcal and other forms of meningitis and reduce associated morbidity and mortality</td>
<td>Identify symptoms of <strong>headache, confusion or visual disturbances</strong>. 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 <strong>lumbar puncture</strong>. <strong>Defer ART if meningitis is confirmed as outlined in “Medical Reasons to Defer ART”</strong> on page 3</td>
</tr>
<tr>
<td>Component of the Baseline Clinical Evaluation</td>
<td>Purpose</td>
<td>Further Action Required</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>---------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Screen for active depression, other mental health issues or substance abuse</td>
<td>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</td>
<td>Screen for symptoms of depression, psychosis, and substance abuse</td>
</tr>
<tr>
<td>Screen for major chronic non-communicable diseases (NCDs) (diabetes, hypertension, epilepsy)</td>
<td>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</td>
<td>Do blood pressure (BP), and urine dipstick 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</td>
</tr>
<tr>
<td>Screen for pregnancy and ask if planning to conceive</td>
<td>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</td>
<td>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</td>
</tr>
<tr>
<td>Symptom screen for sexually transmitted infections (STIs)</td>
<td>To identify and treat STIs in sexually active clients</td>
<td>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?”</td>
</tr>
<tr>
<td>Neurodevelopmental screen</td>
<td>To identify children with neurodevelopmental delay requiring intervention/referral and follow-up</td>
<td>N/A</td>
</tr>
<tr>
<td>WHO clinical stage</td>
<td>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:</td>
<td></td>
</tr>
</tbody>
</table>

**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 CPT” on page 7)
Baseline Laboratory Evaluation for Adults and Adolescents, Pregnant Women, and Children includes the following:

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

<table>
<thead>
<tr>
<th>Laboratory evaluation</th>
<th>Purpose</th>
<th>Adolescents (10-19 years) and Adults</th>
<th>Pregnant Women</th>
<th>Children (&lt; 10 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirm HIV test result</td>
<td>To confirm HIV status for those without documented HIV status</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>CD4 cell count/ %</td>
<td>To identify eligibility for CPT</td>
<td>See “Indications for starting and stopping cotrimoxazole” in table on page 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>To identify eligibility for cryptococcal antigen (CrAg) screening</td>
<td>A reflex CrAg test will be done automatically by the laboratory on all CD4 counts &lt; 100 cells/μL</td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>Creatinine and eGFR if TDF used</td>
<td>To assess renal insufficiency</td>
<td>See table titled “Assessing Renal Function” on page 7</td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>Haemoglobin (Hb)</td>
<td>To identify and manage anaemia; to determine eligibility for zidovudine (AZT) where necessary</td>
<td>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 accordingly¹</td>
<td>Treat with ferrous sulphate tds if Hb &lt; 10 g/dL. Refer if &lt; 8 g/dL and symptoms, if anaemia diagnosed at 36 weeks gestation or later, or if no response to treatment</td>
<td>Children &lt; 5 years: Treat with iron supplements and deworm the child¹. Children &gt; 5 years: Do FBC. Characterise according to MCV and manage accordingly²</td>
</tr>
<tr>
<td>GeneXpert</td>
<td>To diagnose TB</td>
<td>Only for those clients with a positive TB symptom screen</td>
<td>Regardless of TB symptoms, routinely do a TB GeneXpert for all HIV-positive women at first visit in antenatal clinic, due to the lower sensitivity of the TB symptom screen in pregnant women</td>
<td>Only for those with a positive TB symptom screen</td>
</tr>
<tr>
<td>Cryptococcal antigen test (CrAg) if CD4 &lt; 100 cells/μL</td>
<td>To identify asymptomatic clients who need pre-emptive fluconazole treatment</td>
<td>A reflex CrAg test will be done automatically by the laboratory on all CD4 counts &lt; 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</td>
<td>All pregnant women with a positive CrAg should be referred for a lumbar puncture, regardless of symptoms. The results of the lumbar puncture and further management should be discussed with an expert, or one of the helplines provided on page 16</td>
<td>N/A</td>
</tr>
<tr>
<td>Cervical cancer screening</td>
<td>To identify women with cervical lesions and manage appropriately</td>
<td>All HIV-positive women should be screened for cervical cancer at diagnosis and subsequently every 3 years if the screening test is negative. If positive, she should be referred for colposcopy and further interventions</td>
<td>Pregnancy does not preclude screening for cervical cancer and it can be performed up to 20 weeks of gestation. However, pap smear results may be more difficult to interpret in pregnancy, and any abnormal smears should be repeated at 6 to 12 weeks after delivery.</td>
<td>N/A</td>
</tr>
<tr>
<td>HBsAg</td>
<td>To identify those co-infected with hepatitis B (HBV)</td>
<td>If positive, exercise caution in stopping TDF-containing regimens, to prevent hepatitis flares</td>
<td></td>
<td>N/A</td>
</tr>
</tbody>
</table>

¹ As outlined in the PHC EML 2018
### Assessing Renal Function

<table>
<thead>
<tr>
<th>Age/pregnancy Status</th>
<th>What must be measured?</th>
<th>Acceptable level for TDF use</th>
<th>Counahan Barratt formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 10 and &lt; 16 years of age</td>
<td>eGFR using Counahan Barratt formula</td>
<td>&gt; 80 mL/min/1.73 m²</td>
<td>eGFR (mL/min/1.73 m²) = ( \frac{\text{height [cm]} \times 40}{\text{creatinine [μmol/L]}} )</td>
</tr>
<tr>
<td>Adults and adolescents ≥ 16 years</td>
<td>eGFR using MDRD equation</td>
<td>&gt; 50 mL/min/1.73m²</td>
<td></td>
</tr>
<tr>
<td>Pregnant women</td>
<td>Absolute creatinine level</td>
<td>&lt; 85 μmol/L</td>
<td></td>
</tr>
</tbody>
</table>

1. Modification of Diet in Renal Disease Study (MDRD) equation. The MDRD formula is automatically calculated by the laboratory for those 18 years and older. For assistance in manually calculating the eGFR for adolescents between 16 and 18 years of age, please contact one of the helplines provided on page 16. 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)

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

### 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.

<table>
<thead>
<tr>
<th>Category of Client</th>
<th>Specific Eligibility Criteria</th>
<th>Treatment and Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult or adolescent &gt; 15 years (non-pregnant)</td>
<td>Any CD4 count. Exclude active liver disease, alcohol abuse, or known hypersensitivity to isoniazid</td>
<td>Isoniazid, oral, 300 mg daily for 12 months and pyridoxine 25 mg daily</td>
</tr>
<tr>
<td>Children who are contacts of index TB cases</td>
<td>Children &lt; 5 years (regardless of HIV status), and children 5-14 years who are HIV-positive</td>
<td>Isoniazid, oral, 10 mg/kg/day for 6 months (maximum dose 300 mg daily) and pyridoxine daily</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>Eligible if CD4 count ≤ 100 cells/μL. If CD4 &gt; 100 cells/μL, defer TPT till 6 weeks after delivery*</td>
<td>Isoniazid, oral, 300 mg daily for 12 months and pyridoxine 25 mg daily</td>
</tr>
</tbody>
</table>

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

---

**Lifestyle Interventions**

All clients should be encouraged to apply the following lifestyle changes as appropriate: Maintain an ideal weight, i.e. BMI < 25 kg/m². Overweight clients with BMIs > 25 kg/m² 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**

<table>
<thead>
<tr>
<th>Interacting Drug</th>
<th>Effect of Co-Administration</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin</td>
<td>Dolutegravir</td>
<td>Double DTG dose to 50 mg 12-hourly. If on TLD FDC, add DTG 50 mg 12 hours after TLD dose</td>
</tr>
<tr>
<td>Polyvalent cations (Mg²⁺, Fe²⁺, Ca²⁺, Al³⁺, Zn²⁺) e.g. antacids, sucralfate, multivitamin and nutritional supplements</td>
<td>Dolutegravir</td>
<td>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. 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</td>
</tr>
<tr>
<td>Anticonvulsants: • Carbamazepine • Phenobarbital • Phenytoin</td>
<td>Dolutegravir</td>
<td>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 if an alternative anticonvulsant cannot be used</td>
</tr>
<tr>
<td>Metformin/DTG</td>
<td>Metformin</td>
<td>DTG increases metformin levels. Maximum metformin dose 500 mg 12-hourly</td>
</tr>
</tbody>
</table>

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,
the Liverpool HIV iChart application for smart phones, or any of the helplines provided on page 16
Adult Women and Adolescent Girls ≥ 35 kg\(^1\) and ≥ 10 years of Age

**Women or Adolescent Girls of Childbearing Potential?**

- **YES**
- **NO**

**Determine current pregnancy status and fertility intentions**

- **Pregnant, up to 6 completed weeks of gestation, or actively wanting to conceive in the near future\(^2\)**
- **All other WOC\(^3\), including:**
  - Pregnant, from 7 weeks gestational age onwards
  - Not pregnant, and not currently desiring to become pregnant

**Provide all necessary information on DTG and EFV-based regimens including the risk of NTDs for this and subsequent pregnancies**

- **TEE recommended**
- **TLD recommended**

**Client makes an informed choice after understanding risks and benefits**

- **TEE \(^{1,4}\)**
- **TLD \(^{1,5,6}\)**

Adult Men and Adolescent Boys ≥ 35 kg and ≥ 10 years of Age

**For further detail on transitioning between regimens, see “Switching Stable Clients on ART Between First-Line Regimens” on page 13-14**

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

- **Birth to < 4 weeks of age\(^7\):**
  - 2.5 kg
  - 3 kg
  - Neonates
  - AZT + 3TC + NVP

- **≥ 4 wks of age, and ≥ 42 wks gestational age\(^8\):**
  - 20 kg
  - Or < 10 years of age
  - Infants and Children
  - ABC + 3TC + LPV/r

- **20 kg**
  - Children
  - ABC + 3TC + DTG

- **≥ 4 wks of age, and ≥ 42 wks gestational age\(^8\):**
  - 35 kg
  - and ≥ 10 years of age
  - Transition to Adult and Adolescent Regimens

**Transition does not require a VL before switching**

**Transition requires a VL < 50 c/mL in the last 6 months**

**Transition requires a VL < 50 c/mL in the last 6 months. Ensure adequate renal function\(^9\)**

1. For adolescent girls who weigh less than 35 kg, replace tenofovir with abacavir (ABC)
2. Women wanting to conceive should be started on folate and should be counselled to defer attempts to conceive until they are virally suppressed. See also “Contraception and Safe Conception” on page 9 of the PMTCT guideline.
3. Women should be provided a choice of contraceptive options (which includes condoms, oral contraceptives, implants, injectables, and IUCDs)
4. Women who choose to use TEE around the time of conception can be offered a switch to TLD if their VL is suppressed at 3-months on ART.
5. Documentation that the woman has been counselled and consents to receive DTG must be included in the patient’s chart/file.
6. If a woman’s fertility intentions change and she is concerned about the risk of NTDs, she can be offered a switch from TLD to TEE, provided that she has a suppressed VL in the last 6 months
7. For preterm neonates and neonates with birth weight < 2.5 kg, or neonates with severe anaemia, obtain advice from an expert or through one of the helplines provided on page 16
8. For infants ≥ 4 weeks of age, ≥ 42 weeks gestational age, but weighing less than 3 kg, a paediatric expert should be consulted to determine the appropriate regimen
9. Before switching to TDF, ensure adequate renal function by checking eGFR/creatinine as outlined in table on page 7
ART Initiation in Women and Adolescent Girls Diagnosed with HIV during Labour

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

Lifelong ART should be initiated the following day. TLD and a contraceptive method is recommended. However, she should be provided with all necessary information on DTG and EFV-based regimens including the risk of NTDs, and enabled to make an informed choice. Provide her with a choice of contraceptive options as desired.

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

Re-initiating ART in Clients who have Interrupted Treatment

Take a thorough history including:

1) which drugs the patient was taking, and for how long;
2) the reasons for stopping ART;
3) side-effects; and
4) any information on VL measurements whilst on ART.

- If the patient was well on their first-line regimen, side-effects were not the reason for stopping ART, and their VL was suppressed (or no VL result is available), restart the first-line regimen they were on at the time of interruption. Do a VL after 3 months on ART. The majority of clients should suppress by 3 months on ART. For those that remain unsuppressed, provide enhanced adherence support and repeat the VL at 6 months on ART (3 months later). If their VL is < 1000 c/ml at either the 3- or 6-month VL, they can be offered a single drug switch to DTG. If their VL is > 1000 c/ml at 6 months on ART, manage the virological failure in accordance with their specific regimen (see the “Management of VL results” algorithm on page 16). If in doubt, contact one of the helplines provided on page 16.
- If the client stopped treatment due to side-effects, manage as outlined in the comprehensive Consolidated HIV Guidelines document, or contact one of the helplines provided on page 16.
- If the client was failing but is still clinically well, consider restarting their original first line therapy.
- If the client is ill, consider a new regimen, consulting an experienced clinician as necessary.
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:

1. **The timing of ART initiation**
   (see “Indications to defer ART” on page 3)

2. **Drug selection** in clients who are not yet on ART when TB treatment is initiated

3. **Drug levels**, due to significant **drug interactions** that reduce ART concentrations in the blood

4. **Adherence**, due to increased pill burden

5. **Side-effects** due to overlapping toxicities, e.g., hepatic toxicity

**Efavirenz** has no significant interaction with rifampicin

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

In both these situations, the EFV-containing regimen should be continued until two weeks after TB treatment is completed. Thereafter, EFV can be switched to DTG, provided that the process has been followed as outlined in “Switching Stable Clients on ART Between First-Line Regimens” on page 14.

**Drug Interactions**

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

- **Neonates**
  - ART regimen: AZT + 3TC + NVP
  - Significant drug interaction: Rifampicin + NVP

- **Infants and Children**
  - ART regimen: ABC + 3TC + LPV/r
  - Significant drug interaction: Rifampicin + LPV/r

- **Children**
  - ART regimen: ABC + 3TC + DTG
  - Significant drug interaction: Rifampicin + DTG

**Measures to counteract drug interactions with rifampicin**

- Seek expert advice

**LPV/r tablets**: Double-dose LPV/r tablets
(See Dosing Chart on page 20). Tablets can be used only if the child is able to swallow whole LPV/r tablets (tablet must not be crushed, broken or chewed). If the child is unable to tolerate LPV/r at double doses, consult one of the helplines provided on page 16. LPV/r solution: Super-boosting with additional ritonavir solution or ritonavir powder: maintain standard LPV/r dose but add additional ritonavir twice daily as per Dosing Chart on page 20. If no ritonavir solution or powder is available, consult an expert for a suitable alternative. Ritonavir solution has a shelf-life of only 6 months, whereas ritonavir powder has a shelf-life of 36 months. Note that ritonavir 100 mg tablets must not be crushed, broken or chewed.

**Boosting of DTG required**
The dosing frequency of DTG should be increased to 50 mg 12-hourly. If on TLD FDC, then add DTG 50 mg 12 hours after TLD dose

**Continue boosting the ART regimen until 2 weeks after stopping rifampicin**
### 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

<table>
<thead>
<tr>
<th>Current Regimen</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF + 3TC/FTC + EFV/NVP</td>
<td>Switch to TDF + 3TC/FTC + DTG</td>
</tr>
<tr>
<td>AZT/ABC + 3TC + EFV/NVP</td>
<td>Switch to AZT/ABC + 3TC + DTG</td>
</tr>
</tbody>
</table>

### 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 | Provide information on the risks and benefits of DTG, and the use of contraception in WOCP (see page 8). Enable the client to make an informed decision. |
| VL 50 - 999 c/mL | Do a thorough assessment of the cause of an elevated VL as outlined on page 16. Implement interventions and provide enhanced adherence support. Repeat VL in 3 months |
| VL ≥ 1000 c/mL | Ensure that the elevated VL is correctly managed according to the VL results management algorithm on page 16. Do not switch to DTG at this time |

#### Client chooses to switch to DTG

- If current regimen is TDF + 3TC/FTC + EFV/NVP: Switch to TDF + 3TC/FTC + DTG
- If current regimen is AZT/ABC + 3TC + EFV/NVP: Switch to AZT/ABC + 3TC + DTG

#### Client chooses to remain on their current regimen

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

Only switch a **stable pregnant woman** on ART from EFV to DTG if her VL is < 50 copies/mL, and she is **not longer in the first 6 weeks of pregnancy**. A switch to DTG needs to be preceded by WOCP being given all necessary information on DTG and EFV-based regimens including the risk of NTDs. Discuss postpartum contraceptive options and allow her to make an informed choice.

- 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.*
- *Clients on CCMDD can be considered for a switch to TLD and remain on CCMDD if they have a VL < 50 c/mL in the last 6 months. For more information see the TLD Transition Guide for Implementers, or the CCMDD SOP: Changing of ARV regimen from TEE to TLD (CCMDD SOP-16).*

1. Discuss and provide sexual and reproductive health services for the sexually active adolescent/adult.
2. Assess the reason for exclusion of TDF from the NRTI backbone. If TDF was excluded due to 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

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 - 999 c/mL

Do a thorough assessment of the cause of an elevated VL as outlined on page 16
Implement interventions and provide enhanced adherence support
Repeat VL in 3 months

VL 50 - 999 c/mL

VL ≥ 1000 c/mL

Ensure that the elevated VL is correctly managed according to the VL results management algorithm on page 16
Do not switch to DTG at this time

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

If weight reaches 35 kg or more, and VL < 50 c/mL in the last 6 months, and renal function is normal³

ABC + 3TC + DTG²

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

TDF³ + 3TC + DTG²

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

Weight ≥ 35 kg and age ≥ 10 years, and renal function normal³

Renal function abnormal

*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.

¹ 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.

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

³ Before switching to TDF, ensure adequate renal function by checking eGFR/creatinine as outlined in the table “Assessing Renal Function” on page 7.
The following components should be included in the clinical assessment:

1. **Viral load**
   - Should be measured to timeously detect problems with adherence or treatment failure
   - At month 6 on ART and month 12 on ART
   - Thereafter, if virally suppressed, repeat every 12 months
   - Remember, an elevated VL is a medical emergency! Assess and manage according to the “Management of VL results” algorithm on page 16

2. **The CD4 count**
   - Should be measured to monitor susceptibility to opportunistic infections and eligibility for CPT
   - At month 12 on ART
   - Thereafter, repeat every 6 months until client meets criteria to discontinue CPT. Stop CD4 monitoring if client’s VL remains below 1000 c/mL.
   - If VL >1000 c/mL, monitor CD4 “count every 6 months.

3. **Screen for TB and other OIs**
   - To diagnose and provide treatment; to adjust ART regimen if required; to determine if TB preventive therapy is required
   - Screen for pregnancy and ask if planning to conceive as outlined in the table for “Baseline Clinical Evaluation” on page 5

4. **Weight (adults)**
   - An assessment of trends in weight in adults
   - Remember to adjust ART dosage according to weight!

5. **Growth and neurodevelopment (children)**
   - An assessment of trends in weight, height, head circumference, and neurodevelopment
   - Remember to adjust ART dosage according to weight!

6. **Side-effects and ART toxicities**
   - Can affect adherence and endanger the client’s health
   - Drug side-effects
     - Ask about side-effects at each visit (e.g. sleep or gastrointestinal disturbances)
   - TDF-induced nephrotoxicity
     - If on TDF, do creatinine and eGFR* at months 3, 6 and 12
     - Thereafter, repeat every 12 months
   - Dyslipidaemia
     - If on a PI-based regimen (LPV/r, ATV/r, DRV/r), do total cholesterol and triglycerides (TGs) at month 3
     - If above acceptable range, do fasting cholesterol and TGs and if still above acceptable range, obtain expert advice
   - Anaemia and neutropaenia
     - If on AZT, do a full blood count and differential white cell count at months 3 and 6
     - Thereafter, repeat if clinically indicated

---

### *Assessing Renal Function*

<table>
<thead>
<tr>
<th>Age/pregnancy status</th>
<th>What must be measured?</th>
<th>Acceptable level for TDF use</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 10 and &lt; 16 years of age</td>
<td>eGFR using Counahan Barratt formula</td>
<td>&gt; 80 mL/min/1.73 m²</td>
</tr>
<tr>
<td>Adults and adolescents ≥ 16 years</td>
<td>eGFR using MDRD equation</td>
<td>&gt; 50 mL/min/1.73m²</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>Absolute creatinine level</td>
<td>&lt; 85 μmol/L</td>
</tr>
</tbody>
</table>

---

1. Modification of Diet in Renal Disease Study (MDRD) equation. The MDRD formula is automatically calculated by the laboratory for those 18 years and older. For assistance in manually calculating the eGFR for adolescents between 16 and 18 years of age, please contact one of the helplines provided on page 16. 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.
Management of Viral Load Results in Infants, Children, Adolescents and Adults

Routine VL monitoring at 6 months on ART, 12 months on ART, and 12-monthly thereafter

- VL < 50 c/mL
  - Continue routine VL monitoring

- VL 50 - 999 c/mL
  - Continue routine VL monitoring

- VL ≥ 1000 c/mL
  - Do a thorough assessment of the cause of an elevated VL. Consider the possibility of:
    A. Adherence problems
    B. Bugs (Intercurrent infections)
    C. Incorrect ART dosage
    D. Drug Interactions
    E. Resistance
  - Implement interventions to re-suppress the VL, including enhanced adherence support as outlined in the Adherence Guideline for HIV, TB and NCDs

Repeat VL after 3 months

- VL < 50 c/mL
  - Continue routine VL monitoring

- VL 50 - 999 c/mL
  - Continue enhanced adherence support Repeat VL in 6 months*

- VL ≥ 1000 c/mL
  - NNRTI-based regimen (EFV/NVP)
    - Consider switching to second-line if virological failure confirmed, i.e. VL ≥ 1000 c/mL on two consecutive occasions and adherence issues addressed
  - INSTI (DTG) or PI-based regimen*
    - Consider switching to second-line if virological failure confirmed, i.e. VL ≥ 1000 c/mL on at least three occasions over the course of two years, or VL ≥ 1000 c/mL with signs of immunological or clinical failure (i.e. declining CD4 and/or opportunistic infections)

* Due to their high genetic barrier, resistance to DTG and PIs develops very slowly. An elevated VL on DTG or LPV/r is therefore more likely to be related to suboptimal adherence. For this reason, a client should be on DTG or LPV/r for at least 2 years before considering a switch to second-line.

Clients who have persistent low grade viraemia of between 50 - 999 c/mL should be discussed with one of the helplines listed below on a case-by-case basis. If the client is still on an NNRTI based regimen, a single drug switch to DTG can be considered as outlined in the switching algorithm on page 13.

For second and third-line regimens, go to page 17

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

- National HIV & TB Health Care Worker Hotline: 0800 212 506
- Right to Care Adult HIV Helpline: 082 957 6698
- Right to Care Paediatric and Adolescent HIV Helpline: 082 352 6642
- KZN Paediatric Hotline: 0800 006 603
Second-Line and Third-Line ART Regimens

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

<table>
<thead>
<tr>
<th>Regimen</th>
<th>First-Line Regimens</th>
<th>Second-Line Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNRTI-based Regimen</td>
<td>TDF + 3TC/FTC + EFV/NVP</td>
<td>TDF + 3TC/FTC + DTG</td>
</tr>
<tr>
<td>INSTI-based Regimen for &gt; 2 years</td>
<td>TDF + 3TC/FTC + LPV/r or ATV/r</td>
<td>AZT/TDF + 3TC/FTC + LPV/r or ATV/r</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resistance Testing</th>
<th>Resistance test not required</th>
<th>Resistance testing may be required under expert consultation 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistance Test Results</td>
<td>Not applicable</td>
<td>No PI resistance</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HBV Co-infection Status 1</th>
<th>HBV-negative</th>
<th>HBV-positive</th>
<th>HBV-positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Regimen</td>
<td>AZT + 3TC/FTC + DTG 2</td>
<td>TDF 3 + AZT + 3TC/FTC + DTG 2</td>
<td>AZT + 3TC/FTC + LPV/r</td>
</tr>
<tr>
<td>If DTG not suitable 2, AZT + 3TC/FTC + LPV/r</td>
<td>TDF 3 + 3TC/FTC + LPV/r 4</td>
<td>TDF + 3TC/FTC + LPV/r 4</td>
<td></td>
</tr>
</tbody>
</table>

**Resistance Test Results**

- Continue current regimen and address adherence. If intolerance to LPV/r is affecting adherence, discuss possible substitutions with an expert.
- Refer to Third-Line Committee. Regimen will be determined by results of resistance test.

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

<table>
<thead>
<tr>
<th>Regimen</th>
<th>First-Line Regimens</th>
<th>Second-Line Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNRTI-based Regimen</td>
<td>ABC/AZT/TDF + 3TC/FTC + EFV/NVP</td>
<td>ABC/AZT/TDF + 3TC/FTC + LPV/r or ATV/r</td>
</tr>
<tr>
<td>PI-based Regimen for &gt; 2 years</td>
<td>ABC/AZT/TDF + 3TC/FTC + LPV/r</td>
<td>ABC/AZT/TDF + 3TC/FTC + DTG</td>
</tr>
<tr>
<td>INSTI-based Regimen for &gt; 2 years</td>
<td>ABC/AZT/TDF + 3TC/FTC + DTG 2</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resistance Testing</th>
<th>Resistance test not required</th>
<th>Resistance test required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistance Test Results</td>
<td>Not applicable</td>
<td>No PI resistance</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight</th>
<th>&lt; 20 kg</th>
<th>≥ 20 kg</th>
<th>&lt; 20 kg</th>
<th>≥ 20 kg</th>
<th>All</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>New Regimen or Other Action Required</th>
<th>2 NRTIs + DTG 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>In consultation with an expert, ensure that at least 1 NRTI is active 3</td>
<td></td>
</tr>
<tr>
<td>If NRTI activity cannot be confirmed, expert will recommend 2 NRTIs + PI/r</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>New Regimen</th>
<th>ABC/AZT + 3TC + LPV/r 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 NRTIs + DTG 2</td>
<td></td>
</tr>
<tr>
<td>In consultation with an expert, ensure that at least 1 NRTI is active 3</td>
<td></td>
</tr>
<tr>
<td>If NRTI activity cannot be confirmed, expert will recommend 2 NRTIs + PI/r. Adherence must be addressed</td>
<td></td>
</tr>
</tbody>
</table>

1. **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.**

2. **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).**

3. From the DAWNING study, DTG was shown to achieve viral suppression when used in combination with two NRTIs, at least one of which was fully active (Aboud M et al., IAS Oral abstract, 2017). It is as yet unknown if DTG will work if combined with two NRTIs, neither of which are fully active.

4. 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.

5. Resistance testing for adults and adolescents failing a DTG-based second-line regimen and who meet the definition of confirmed virological failure may be authorized by an expert on a case-by-case basis. Resistance testing for clients failing a DTG-containing first-line regimen is not indicated.
Protocol for initiation of ART in HIV-infected neonates ≥ 2.5 kg at birth

Infant born to a woman living with HIV
Ensure mother is on ART; Advise on breastfeeding

Initial counselling for mother/caregiver on positive birth HIV PCR and starting ART

Birth HIV PCR test

Positive Birth HIV PCR test
Actively trace and link to care

Baseline Assessment for neonate ≥ 2.5 kg
Clinical review
Bloods: confirmatory HIV PCR, CD4 count/%, FBC/differential count, ALT (Genotype if mother is failing second or third-line ART)

Start ART on same day (if oral feeding is established)
AZT (4 mg/kg/dose BD)
3TC (2 mg/kg/dose BD)
NVP (6 mg/kg/dose BD)

Review at 1 week of treatment:
Clinical review and counselling
Check blood results, including confirmatory PCR

Review at 2 weeks of treatment:
Clinical review and counselling

Review at 1 month of treatment:
Clinical review and counselling
Bloods: FBC/differential count
Start cotrimoxazole prophylaxis
Adjust medication

If ≥ 3 kg:
Switch NVP to LPV/r (Kaletra) and AZT to ABC
Dose ABC, 3TC, LPV/r as per SA NDOH dosing chart

If still < 3 kg:
Switch NVP to LPV/r (Kaletra): 1 ml BD
Dose AZT 12 mg/kg/dose BD, 3TC 4 mg/kg/dose BD

Review monthly until 6 months of treatment:
Adjust medication using dosing chart
Month 6: Do viral load

VL lower than detectable limit:
Continue ABC, 3TC, LPV/r
Review monthly until 1 year
Repeat VL and CD4

VL detectable:
Continue ABC, 3TC, LPV/r
Adherence strengthening
Review monthly
Repeat VL after 3 months
If VL still detectable discuss with paediatrician

Refer to documents below where numbered in the protocol:
1. Dosage chart if < 28 days of age (see page 19)
2. SA NDOH dosing chart (see page 20)

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 ≥ 2.5 kg (≥ 35 weeks gestational age at birth)

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Lamivudine (3TC)</th>
<th>Zidovudine (AZT)</th>
<th>Nevirapine (NVP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 2.5 - &lt; 3</td>
<td>2 mg/kg/dose TWICE daily (BD)</td>
<td>4 mg/kg/dose TWICE daily (BD)</td>
<td>6 mg/kg/dose TWICE daily (BD)</td>
</tr>
<tr>
<td>≥ 3 - &lt; 4</td>
<td>0.5 mL BD 5 mg BD</td>
<td>0.8 mL BD 8 mg BD</td>
<td>1 mL BD 10 mg BD</td>
</tr>
<tr>
<td>≥ 4 - &lt; 5</td>
<td>1 mL BD 10 mg BD</td>
<td>1.5 mL BD 15 mg BD</td>
<td>2 mL BD 20 mg BD</td>
</tr>
</tbody>
</table>

- 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.

<table>
<thead>
<tr>
<th>Target dose</th>
<th>Available formulations</th>
<th>Weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Atazanavir</strong> (ABC)</td>
<td>3 - 5.9</td>
</tr>
<tr>
<td></td>
<td>Lamivudine (3TC)</td>
<td>6 - 13.9</td>
</tr>
<tr>
<td></td>
<td>Atazanavir / ritonavir (LPV/r)</td>
<td>14 - 24.9</td>
</tr>
<tr>
<td></td>
<td>Lopinavir / ritonavir (LPV/r)</td>
<td>15 - 24.9</td>
</tr>
<tr>
<td></td>
<td>Lopinavir / ritonavir when on rifampicin</td>
<td>16 - 24.9</td>
</tr>
<tr>
<td></td>
<td>Dolutegravir (DTG)</td>
<td>20 - 29.9</td>
</tr>
<tr>
<td></td>
<td>Katena (EFV)</td>
<td>25 - 34.9</td>
</tr>
<tr>
<td></td>
<td>Abacavir</td>
<td>35 - 39.9</td>
</tr>
<tr>
<td></td>
<td>Dolutegravir (DTG)</td>
<td>≥ 40</td>
</tr>
</tbody>
</table>

**Atazanavir + ritonavir should not be used in children/adolescents on treatment with rifampicin, obtain expert advice.**

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

Children weighing 20-29.9 kg may also be dosed with LPV/r 200/50 mg adult tabs: 2 tabs am + 1 tab pm.

**TLD, tenofovir/lamivudine/dolutegravir; TEE, tenofovir/emtricitabine/efavirenz.**

### Drug Dosing Chart for Children (2019)

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Cotrimoxazole Dose</th>
<th>Multivitamin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 - 5.9</td>
<td>2.5 ml od</td>
<td>2.5 ml od</td>
</tr>
<tr>
<td>6 - 13.9</td>
<td>5 ml or 1 tab od</td>
<td>5 ml od</td>
</tr>
<tr>
<td>14 - 24.9</td>
<td>10 ml or 1 tab od</td>
<td>10 ml od</td>
</tr>
<tr>
<td>≥ 25</td>
<td></td>
<td>2 tabs od</td>
</tr>
</tbody>
</table>

### Available formulations

- **ABC**: Atazanavir capsules, 300 mg; Atazanavir / ritonavir (LPV/r) solution; Atazanavir / ritonavir when on rifampicin.
- **3TC**: Lamivudine capsules, 60 mg; Lamivudine tablets, 150 mg.
- **LPV/r**: Lopinavir / ritonavir capsules, 400 mg; Lopinavir / ritonavir tablets, 200 mg.
- **DTG**: Dolutegravir capsules, 50 mg; Dolutegravir tablets, 100 mg.
- **EFV**: Efavirenz capsules, 200 mg; Efavirenz tablets, 300 mg.
- **TLD**: Tenofovir / lamivudine / dolutegravir capsules, 1 x 300 mg; Tenofovir / lamivudine / dolutegravir tablets, 2 x 150 mg.

### Available formulations

- **ABC**: Atazanavir capsules, 300 mg; Atazanavir / ritonavir (LPV/r) solution; Atazanavir / ritonavir when on rifampicin.
- **3TC**: Lamivudine capsules, 60 mg; Lamivudine tablets, 150 mg.
- **LPV/r**: Lopinavir / ritonavir capsules, 400 mg; Lopinavir / ritonavir tablets, 200 mg.
- **DTG**: Dolutegravir capsules, 50 mg; Dolutegravir tablets, 100 mg.
- **EFV**: Efavirenz capsules, 200 mg; Efavirenz tablets, 300 mg.
- **TLD**: Tenofovir / lamivudine / dolutegravir capsules, 1 x 300 mg; Tenofovir / lamivudine / dolutegravir tablets, 2 x 150 mg.

### Available formulations

- **ABC**: Atazanavir capsules, 300 mg; Atazanavir / ritonavir (LPV/r) solution; Atazanavir / ritonavir when on rifampicin.
- **3TC**: Lamivudine capsules, 60 mg; Lamivudine tablets, 150 mg.
- **LPV/r**: Lopinavir / ritonavir capsules, 400 mg; Lopinavir / ritonavir tablets, 200 mg.
- **DTG**: Dolutegravir capsules, 50 mg; Dolutegravir tablets, 100 mg.
- **EFV**: Efavirenz capsules, 200 mg; Efavirenz tablets, 300 mg.
<table>
<thead>
<tr>
<th>ARV Drug</th>
<th>Formulations (as used in dosing chart)</th>
<th>Can tablets be split/crushed if unable to swallow?</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir (ABC)</td>
<td>Oral solution: 20 mg/ml Tablets: 60 mg, 300 mg FDC tablet: ABC/3TC 600/300 mg</td>
<td>Tablets: YES Limited data on FDC, preferably swallow whole or use individual drugs.</td>
<td>Hypersensitivity reaction (fever, rash, GIT &amp; respiratory symptoms) may occur during first 6 weeks of therapy very uncommon in black African patients. Symptoms typically worsen in the hours immediately after the dose and after each subsequent dose. Caregivers or patients should discuss symptoms early with the clinician rather than stopping therapy. Stop ABC permanently if hypersensitivity reaction has occurred.</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>Oral solution: 10 mg/ml Tablets: 150 mg; FDC tablets: ABC/3TC 600/300 mg, TLD 300/300/50 mg</td>
<td>Tablets and FDC: YES Capsules: YES. Open and add to a small amount of soft food/liquid and ingest immediately.</td>
<td>Well tolerated, adverse-effects uncommon. Pure red cell aplasia causing anaemia can occur but is very rare.</td>
</tr>
<tr>
<td>Zidovudine (AZT)</td>
<td>Oral solution: 10 mg/ml Tablets: 100 mg, 300 mg Capsules: 100 mg FDC tablet: AZT/3TC 300/150 mg</td>
<td></td>
<td>Avoid or use with caution in neonates or children with anaemia (Hb &lt; 8 g/dl) due to potential to cause bone marrow suppression.</td>
</tr>
<tr>
<td>Tenofovir (TDF)</td>
<td>Tablets: 300 mg FDC tablets: TDF/FTC 300/200 mg, TEE 300/200/600 mg, TDF/3TC/EFV 300/300/600 mg, TLD 300/300/50 mg</td>
<td>Data is lacking: preferably swallow whole or use individual drugs.</td>
<td>TDF may be prescribed for adolescents ≥ 10 years of age AND ≥ 35 kg body weight after ensuring adequate renal function by checking eGFR/creatinine using the appropriate formula (refer to 2019 ART Clinical Guidelines). TDF is usually prescribed as part of an FDC tablet: TDF/FTC, TDF/FTC/EFV, TDF/3TC/EFV or TDF/3TC/DTG. To assess for TDF-induced nephrotoxicity, do creatinine and eGFR at months 3, 6 and 12 and thereafter repeat every 12 months.</td>
</tr>
<tr>
<td>Lopinavir/ritonavir (LPV/r)</td>
<td>Oral solution: 80/20 mg/ml Tablets: 200/50 mg, 100/25 mg</td>
<td>Tablets: NO</td>
<td>Oral solution should be refrigerated/stored at room temperature (if &lt; 25°C) for up to 6 weeks. Preferably administer oral solution with food as increases absorption. Strategies to improve tolerance and palatability of oral solution: coat mouth with peanut butter, dull taste buds with ice, follow dose with sweet foods. LPV/r has many drug-drug interactions.</td>
</tr>
<tr>
<td>Ritonavir (RTV)</td>
<td>Oral solution: 80 mg/ml Oral powder: 100 mg/packet Tablets: 100 mg</td>
<td>Must be swallowed whole and not divided, crushed or chewed.</td>
<td>Ritonavir oral solution should be stored at room temperature. It’s shelf-life is approximately 6 months. Strategies to improve tolerance and palatability of oral solution: coat mouth with peanut butter, dull taste buds with ice, follow dose with sweet foods. Each 100 mg packet of RTV powder should be mixed with a small amount of water or soft food and immediately ingested. RTV has many drug-drug interactions.</td>
</tr>
<tr>
<td>Atazanavir (ATV)</td>
<td>Capsules: 150 mg, 200 mg</td>
<td>Capsules: NO Must be swallowed whole and not divided, crushed or chewed.</td>
<td>ATV is used in combination with RTV which must be dosed separately as a co-formulation is not available. May cause un conjugated hyperbilirubinaemia resulting in jaundice, but this does not indicate hepatic toxicity and is not a reason to discontinue the drug unless it is worrying the patient. Consider drug-drug interactions.</td>
</tr>
<tr>
<td>Dolutegravir (DTG)</td>
<td>Tablets: 50 mg FDC tablet: TLD 300/300/50 mg</td>
<td>Tablet: YES</td>
<td>Data on crushing FDC tablet is lacking: swallow whole or use individual drugs.</td>
</tr>
<tr>
<td>Efavirenz (EFV)</td>
<td>Capsules: 50 mg, 200 mg Tablets: 50 mg, 200 mg, 600 mg FDC tablet: TEE 300/200/600 mg</td>
<td>Tablets: NO Must be swallowed whole and not divided, crushed or chewed. Capsules: YES. Open and add to small amount of soft food and ingest immediately.</td>
<td>Best given at bedtime to reduce CNS side-effects, especially during first 2 weeks. Consider drug-drug interactions.</td>
</tr>
</tbody>
</table>

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

EMU: Antiretroviral interactions table (http://www.mic.uct.ac.za) OR www.hiv-druginteractions.org/checker OR the Liverpool HIV/Chart application for smartphones, or any of the helplines: National HIV and TB Health Care Worker Hotline: 0800 212 506 or Right to Care Paediatric and Adolescent HIV Helpline: 082 352 6642 and KZN Paediatric Hotline: 0800006 603
Other Resources and Important Information

Adverse Drug Reactions

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

Drug Stock-outs

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

Resources for Clinical Management and Drug Interactions

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

Right to Care Paediatric 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.

Graphics provided by www.Freepik.com
Abbreviations

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
CCMDD Central Chronic Medicines Dispensing and Distribution
CM Cryptococcal meningitis
CNS Central nervous system
CPT Cotrimoxazole preventive therapy
CrAg Cryptococcal Antigen
CVS Cardiovascular
DILI Drug-induced liver injury
DR Drug-resistant
DS Drug-sensitive
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