Western Cape Government

Health

The Western Cape Consolidated Guidelines for HIV Treatment: Prevention of Mother- to-Child Transmission of HIV (PMTCT), Children, Adolescents and Adults 2020

The Western Cape Consolidated Guidelines for HIV Treatment: Prevention of Mother-to- Child Transmission of HIV (PMTCT), Children, Adolescents and Adults

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The WC guidelines are based on the 2014 and 2019 SA National consolidated guidelines for the prevention of mother- to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults & the 2019 National Abridged ART Clinical and PMTCT Guidelines

Acknowledgement goes to members of the Adult and Paediatric HAST policy advisory groups and the Medicines Information Centre, UCT for their valuable input and comment.

Summary of Changes in New Consolidated Guidelines

New section on Dolutegravir	New fixed dose combination (TLD) and single dose dolutegravir (DTG) for children, adolescents and adults in 1st & 2nd line regimens. Specific information on Dolutegravir-related side effects, dosing and drug interactions and guidelines on switching to DTG (section 2).
Change in CD4 monitoring schedule for children, adolescents and adults on ART	Baseline and all at month 12. Then: Repeat CD4 every 6 months until meet criteria to discontinue CPT . If at any later stage VL ≥1000 c/mL on 2 consecutive tests, repeat CD4 every 6 months to monitor for immunological failure
Change to TPT recommendations for HIV positive pregnant women : defer to 6 weeks after delivery if CD4≥100	HIV positive pregnant women in whom TB is excluded are eligible for 12 months of TPT- initiate in pregnancy if CD4<100, defer to 6 weeks post-delivery if CD4≥100. Do a CD4 count for all HIV positive pregnant women at the first ANC visit in order to assess eligibility for TPT. No TST required
Universal TB testing with GeneXpert Ultra for HIV positive pregnant women	All HIV positive pregnant women must be screened for clinical symptoms of TB AND send two sputum specimens for GeneXpert Ultra test regardless of whether or not TB symptoms are present
Medical indications to defer ART: Diagnosis of Drug Sensitive (DS) TB at a non-neurological site (eg. pulmonary TB, abdominal TB, TB lymphadenitis)	If CD4 ≥50 cells/µl, initiate ART 8 weeks after starting TB treatment
Medical indications to defer ART: Diagnosis of Drug Resistant (DR) TB at a non-neurological site (eg. pulmonary TB, abdominal TB, TB lymphadenitis)	Initiate ART after 2 weeks of TB treatment when the client's symptoms are improving, and TB treatment is tolerated
Medical indications to defer ART: Diagnosis of DS-TB or DR-TB at neurological site (eg. TB meningitis or tuberculoma)	Defer ART until 4-8 weeks after start of TB treatment
New section on Screening & Management of Syphilis During Pregnancy & Breastfeeding	Guidelines on primary prevention of syphilis and preventing disease transmission from mother to infant as standard of routine care (section 3.3)
Change in Viral Load (VL) monitoring schedule for pregnant & breastfeeding women	Do baseline VL for all pregnant clients on ART at first antenatal booking. If VL<50c/mL, repeat VL at delivery. Do not repeat VL every 3 months unless there is a valid clinical indication to do so. Monitor VL for clients with VL≥50c/mL closely (section 3.5). Repeat VL at delivery for all clients on ART. Repeat VL for all clients on ART at 6 months post-delivery- align with infant 6-month HIV PCR test. Repeat VL 6 monthly during breastfeeding.
Management of Pregnant Woman newly diagnosed HIV positive during labour/ at delivery	Give stat dose Nevirapine 200mg (sdNVP) + TLD [Tenofovir 300mg + Lamivudine 300mg+ Dolutegravir 50mg] then Initiate lifelong ART with TLD the next day if no contraindications
HIV testing in HIV-exposed infants	Do routine HIV-PCR test at birth, 10 weeks, 6 months and 6 weeks after last breastfeed. No routine test at 18 weeks & 9 months any longer.
Initial positive HIV-PCR test result in infants <18 months to be confirmed with second HIV-PCR test	Use of viral load test to confirm HIV-PCR result no longer recommended.
Universal HIV testing for children at 18 months	Test all children who are not known HIV positive at 18 months for HIV regardless of exposure status
New recommendations for Post-Exposure Prophylaxis (PEP) in HIV-Exposed Infants	All HIV-exposed infants should receive post- exposure prophylaxis (PEP) with nevirapine (NVP) + zidovudine (AZT) post-delivery (section 4). Review results of maternal delivery viral load and infant PCR result at post-natal visit. If infant HIV PCR negative, categorise risk of HIV transmission at birth as high (maternal delivery VL> 1000 c/mL) or low (maternal delivery VL< 1000 c/mL) and review composition and duration of PEP
New section on care of the TB-exposed infant and syphilis-exposed infant	Section 4
Change in indication for resistance testing in adults and children	Infants < 2 years of age who are newly diagnosed as HIV positive are eligible for genotype resistance testing if their mothers were exposed to PI-based ART during pregnancy or breastfeeding. On a PI or DTG based regimen for at least 2 years with virological non-suppression defined as at least three viral load measurements of ≥1000 copies/mL (≥log 3) OR VL>1000 with evidence of clinical or immunological failure. Do genotypic resistance test. If virological non-suppression present but on treatment <2 years, consider doing genotypic resistance test if there is a history of intolerance or poor adherence, non-boosting of a PI-based regimen or no dose adjustment of dolutegravir to overcome a drug interaction
Change in treatment algorithm for the management of cryptococcal meningitis	Induction phase: For adults, adolescents and children, a short-course (one-week) induction regimen with amphotericin B deoxycholate (1.0 mg/kg/day) and flucytosine (100 mg/kg/ day, divided into four doses per day) followed by fluconazole 1200 mg for 1 week.

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Acronym glossary

3TC	Lamivudine
ABC	Abacavir
AIDS	Acquired Immune Deficiency Syndrome
ALD	Zidovudine + Lamivudine + Dolutegravir
ALT	Alanine Aminotransferase
ART	Antiretroviral Treatment
ARV	Antiretroviral
ATV/r	Atazanavir/ritonavir
AZT	Zidovudine
BANC	Basic Antenatal Care
BMI	Body mass index
CBS	Community Based Services
CD4	Cluster of Differentiation 4
CM	Cryptococcal meningitis
Cr	Creatinine
CrCl	Creatinine clearance
DRV/r	Darunavir/ritonavir
d4T	Stavudine
DNA PCR	DNA Polymerase Chain Reaction
DTG	Dolutegravir
eGFR	Estimated glomerular filtration rate
EFV	Efavirenz
ETR	Etravirine
FBC	Full Blood Count
FDC	Fixed dose combination
FTC	Emtricitabine
GFR	Glomerular filtration rate
Hb	Haemoglobin
HBsAg	Hepatitis B Surface Antigen
HIV	Human Immunodeficiency Virus
HTS	HIV Testing Services
InSTI	Integrase strand transfer inhibitor
IPT	Isoniazid Preventive Therapy
IRIS	Immune Reconstitution Inflammatory Syndrome
LPV/r	Lopinavir/ritonavir
MCH	Maternal and Child Health
MDR/XDR-TB	Multi-Drug Resistant/Extensively Drug Resistant Tuberculosis
NRTI	Nucleoside/ Nucleotide reverse transcriptase inhibitor
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NVP	Nevirapine
PHC	Primary Health Care
PI	Protease inhibitor
PLHIV	People Living With HIV/AIDS
PMTCT	Prevention of mother to child transmission
RAL	Raltegravir
SRH	Sexual and Reproductive Health
TB	Tuberculosis
TBM	Tuberculous meningitis
TDF	Tenofovir
TEE	Tenofovir + Emtricitabine + Efavirenz
TLD	Tenofovir + Lamivudine + Dolutegravir
TST	Tuberculin skin test
VL	Viral load
WHO	World Health Organization
WCC	White Cell Count
WOCP	Women of Childbearing Potential

1 INTRODUCTION

1.1 Background

The Western Cape ART and PMTCT guidelines of April 2015 were consolidated to facilitate harmonization of treatment across the life course. Guidelines for initiation of ART in patients with TB and treatment of cryptococcal meningitis were included, as well as indications for the use of Tuberculosis Preventive Therapy (TPT) and Cotrimoxazole Preventive Therapy (CPT). In September 2016, the Universal Test & Treat (UTT) policy was adopted in South Africa, after studies (HPTN052, Temprano and START) found a reduction in serious morbidity of 44–57 % in PLHIV initiating ART early in the course of their disease. Early initiation of ART also has the benefit of reducing transmission of HIV to uninfected partners of people living with HIV (PLHIV).

The main goal of ART is to achieve and maintain virological suppression. In July 2019, the WHO announced that the antiretroviral dolutegravir (an integrase strand inhibitor), in combination with an appropriate nucleoside reverse transcriptase inhibitor (NRTI) backbone, is now the preferred antiretroviral in first and second line regimens for infants and children, adolescents and adults. Dolutegravir has significant advantages, and has been associated with rapid viral suppression and a high genetic barrier to resistance. In addition, side effects are mild and uncommon. This updated guideline includes recommendations for the introduction of DTG- containing regimens to eligible patients at all stages of the life course.

The provision of ART services is guided by the National Strategic Plan on HIV, STIs and TB (NSP 2017 -2022) and the subsequent Provincial Implementation Plan (PIP 2017-2022). The five- year plan provides a roadmap for the journey towards a future where HIV, STIs and TB are no longer public health problems. The NSP calls for a 60% reduction in new HIV infections by 2022. For the Western Cape, that means reducing new HIV infections from 19000 per annum to less than 8000 per annum by 2022. Similarly, the NSP calls for a 30% reduction in new TB infections and in the Western Cape this will mean reducing from 43 000 TB cases per annum to less than 30 000 per annum by 2022.

The targets for Goal 2 are aligned to the 90-90-90 strategies for HIV and TB, which are:

- 90% of Persons living with HIV to know their status; 90% of those who know their status to be initiated on ART; 90% of those on ART to have a suppressed viral load
- 90% of all people who need TB treatment are diagnosed and receive appropriate therapy; 90% of people in key and vulnerable populations are diagnosed and receive appropriate therapy; 90% treatment success rate for drug-sensitive TB
- 75% treatment success rate for drug-resistant TB

The key population groups for HIV services are young women and girls in the age group 15-24 years; people living close to national roads and in informal settlements; young people not attending school and girls who drop out of school before matriculating; people from low socioeconomic groups; uncircumcised men; persons with disabilities and mental disorders; sex workers and their clients; people who abuse alcohol and illegal substances and men who have sex with men and transgender persons. In addition, it recognizes that TB is a major cause of morbidity and mortality in PLHIV, which has led to the adoption of an integrated HIV and TB treatment strategy.

In striving to achieve the goals of Healthcare 2030, the Western Cape has committed to achieving universal quality patient-centered care, which will support adherence of patients on chronic medication. Strategies for providing integrated health services incorporating mental health (MH), non-communicable diseases (NCDs), HIV and tuberculosis (TB) are being implemented. In addition, patients with chronic diseases who are stable on treatment will be offered alternate methods to access medication and maintain adherence to lifelong therapy.

1.2 Goals of the Western Cape ART Programme

- Save lives and improve the quality of life of people living with HIV
- Achieve best health outcomes in the most cost-efficient manner
- Integrate services for HIV, TB, Mental Health, Sexual Reproductive Health, Non-Communicable Diseases and Wellness
- Diagnose HIV earlier and start ART regardless of CD4 count
- Prevent HIV disease progression
- Avert AIDS-related deaths
- Retain patients on lifelong therapy
- Prevent new infections among children, adolescents and adults
- Mitigate the impact of HIV and AIDS
- Strengthen linkages with Community-Based Services

1.3 Specific Objectives

To prioritise initiation of antiretroviral treatment for:

- Patients with CD4 counts ≤ 350 cells/mm_3 or with severe HIV disease (WHO stage 3 or 4)
- Patients co-infected with Tuberculosis (TB)
- Pregnant and breastfeeding women
- To test all HIV exposed children under five years and treat all those found to be infected with HIV
- To promote viral load testing as a preferred approach for monitoring ART success and diagnosing treatment failure
- To standardise first and second line therapy for children, adolescents and adults and reinforce the use of fixed dose combination ART as first line therapy
- To strengthen capacity of nurses to initiate and manage ART for adults patients by increasing the number of authorized Nurse Initiated and Managed ART (NIMART) trained nurses and NIMART mentors
- To increase the number of patients receiving treatment in ARV Clubs in order to manage large numbers of stable patients on life-long ART safely and efficiently
- Adopt an integrated HIV and TB treatment strategy and a strong commitment to providing TPT for all eligible PLHIV

2 Introduction of Dolutegravir- containing ART regimens

2.1 Overview

Dolutegravir (DTG) belongs to a group of antiretroviral drugs called Integrase strand transfer Inhibitors (INSTI). Their mechanism of action is to block the action of the integrase enzyme that inserts the HIV viral DNA into the DNA of the CD4 cell. If integration is blocked, the virus is not able to replicate and viral suppression is attained. DTG has several benefits compared to ARVs in the class of non-nucleoside reverse- transcriptase inhibitors (NNRTI) such as efavirenz (EFV) and nevirapine (NVP):

- Provides rapid viral suppression
- Has high genetic barrier to resistance
- No interaction with hormonal contraceptives
- Side-effects are mild, uncommon and usually self-limiting

Side Effects

- Insomnia, headache, central nervous system (CNS) effects and gastrointestinal effects have been reported
- Advise clients to take DTG in the morning to avoid insomnia.
- Weight gain has emerged as one of the side effects of DTG- in two recent studies (ADVANCE and NAMSAL). ADVANCE found a modest increase in weight was observed in patients on regimens containing and dolutegravir, especially in women and people who had more advanced HIV. All clients should be encouraged to apply lifestyle changes that are appropriate to maintaining an ideal weight, such as a balanced diet, regular exercise and moderate intake of alcohol. Adequate counselling and support on the potential weight gain is of utmost importance.
- Benign increases in creatinine levels due to decreased tubular secretion. Serum creatinine levels increase early in treatment (by less than 15%), and remain stable throughout therapy. This is 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 and neural tube defects (NTDs)

Data from the Tsepamo study in Botswana suggested that there may be an increased risk of NTDs in infants of women using DTG. On review of wider population data, there was a reduction in the estimate of risk, however it remained significant at 0.1% on efavirenz-containing regimens versus 0.3% on dolutegravir-containing regimens. Data from studies in other settings using DTG and other INSTIs is reassuring. The WHO has recommended DTG in combination with an appropriate nucleoside reverse transcriptase inhibitor (NRTI) backbone, as the preferred antiretroviral in 1st and 2nd line regimens for infants and children (with approved dosing), adolescents and adults, including women of child-bearing potential (WOCP).

Women of child bearing potential or any pregnant or breastfeeding woman should receive information about the risks and benefits of EFV and DTG and medical guidance that is appropriate to her situation. She should be allowed to make an informed choice about her treatment and be supported in her choice. This woman-centered approach takes into consideration the needs and perspectives of women and their families and is underpinned by the guiding principles – promoting human rights and gender equality.

The fixed dose combination of TEE (tenofovir disoproxil fumarate (TDF) 300mg + emtricitabine (FTC) 200mg + efavirenz (EFV) 600mg) is recommended for women who are planning to conceive until the end of 6 weeks of pregnancy (when the neural tube closes).
Contraceptive needs should be discussed with women on DTG at every clinical visit.
Women who become pregnant while on DTG should continue on the same regimen if pregnancy is diagnosed after 6 weeks gestation.

2.2 Clients Eligible for DTG-based ART regimens

- ART-naïve clients initiating ART and ART-experienced clients with virological suppression (VL<50c/mL) on a 1st line regimen
- Children 20-35kg: eligible for DTG with appropriate NRTI backbone- NOT including TDF
- Children/ adolescents ≥35kg AND ≥10 years old: eligible for DTG with appropriate NRTI backbone including TDF if renal function adequate
- Men, women and adolescents girls of child-bearing potential and/or breastfeeding: eligible for DTG with appropriate NRTI backbone including TDF if renal function adequate
- Pregnant women: eligible for DTG with appropriate NRTI backbone including TDF if renal function adequate AND completed first 6 weeks of first trimester of pregnancy
- ART-experienced adolescents and children (>20kg) and adults failing treatment on a 1st line NNRTI-based regimen: eligible to switch to DTG-containing regimen including at least one fully active NRTI
- Note: Clients who are currently stable and virologically suppressed (VL<50c/mL) on a 2nd line PI-based regimen should be maintained on that regimen
- Clients on a 3rd line regimen based on results of a genotype resistance test

2.3 Dosing of DTG

- Dolutegravir is available in two formulations:
    - DTG 50mg tablet
    - can be used for children ≥20kg, adolescents and adults
- Fixed dose combination tablet: tenofovir disoproxil fumarate (TDF) 300mg + lamivudine (3TC) 300mg + dolutegravir (DTG) 50mg. This combination is abbreviated as TLD, and can be used for clients ≥35kg AND ≥10 years old
- The standard dose is DTG 50mg daily. DTG may be taken with or without food, preferably in the morning.
- In the fixed dose combination tenofovir 300mg + lamivudine 300mg + DTG 50 mg (TLD), the dose is 1 tablet daily.
- If taking TB treatment containing Rifampicin, double DTG dose to 50 mg twice daily.
- If on TLD, add DTG 50mg as a single dose 12 hour after the TLD dose.

Monitoring on DTG:
No additional monitoring tests are required for DTG. Although serum creatinine levels may increase modestly early in treatment (by less than 15%), it is expected that this will remain stable throughout further treatment and this is not an indication to stop DTG or monitor creatinine levels in addition to the current schedule for clients on TDF.

Table 1: Drug interactions with DTG and recommended dose adjustments

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^{2+}, Fe^{2+}, Ca^{2+}, Al^{3+}, Zn^{2+}) e.g. antacids, sucralfate, multivitamin and nutritional supplements	Dolutegravir ↓	Calcium supplements decrease DTG concentrations if taken together on an empty stomach. To prevent this, DTG and calcium supplements can be taken at the same time if taken with food. 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 2 hours after or 6 hours before DTG.
Anticonvulsants: Carbamazepine Phenobarbital Phenytoin	Dolutegravir ↓	Avoid coadministration if possible. Valproate, 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/DTG	Metformin ↑	DTG increases metformin levels. Maximum metformin dose 500 mg 12-hourly

2.4 Initiating DTG-containing regimens

- A DTG-containing regimen should be initiated in newly diagnosed HIV positive children ≥20 kg, adolescents & adults including women who are pregnant ≥6 weeks gestation and breastfeeding women
- Adolescent girls & women of child-bearing potential: Screen for pregnancy and discuss fertility intentions. Counsel on the risks and benefits of EFV-containing ART versus DTG-containing ART (boxes 1&2). If pregnancy planned in the near future, advise to initiate TEE and consider switching to TLD after 6 weeks gestation. If no pregnancy planned, discuss options for contraception and recommend the use of dual contraception. Initiate TLD and advise her to return for switch to TEE if fertility intentions change.

Box 1: Benefits & risks of using DTG

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

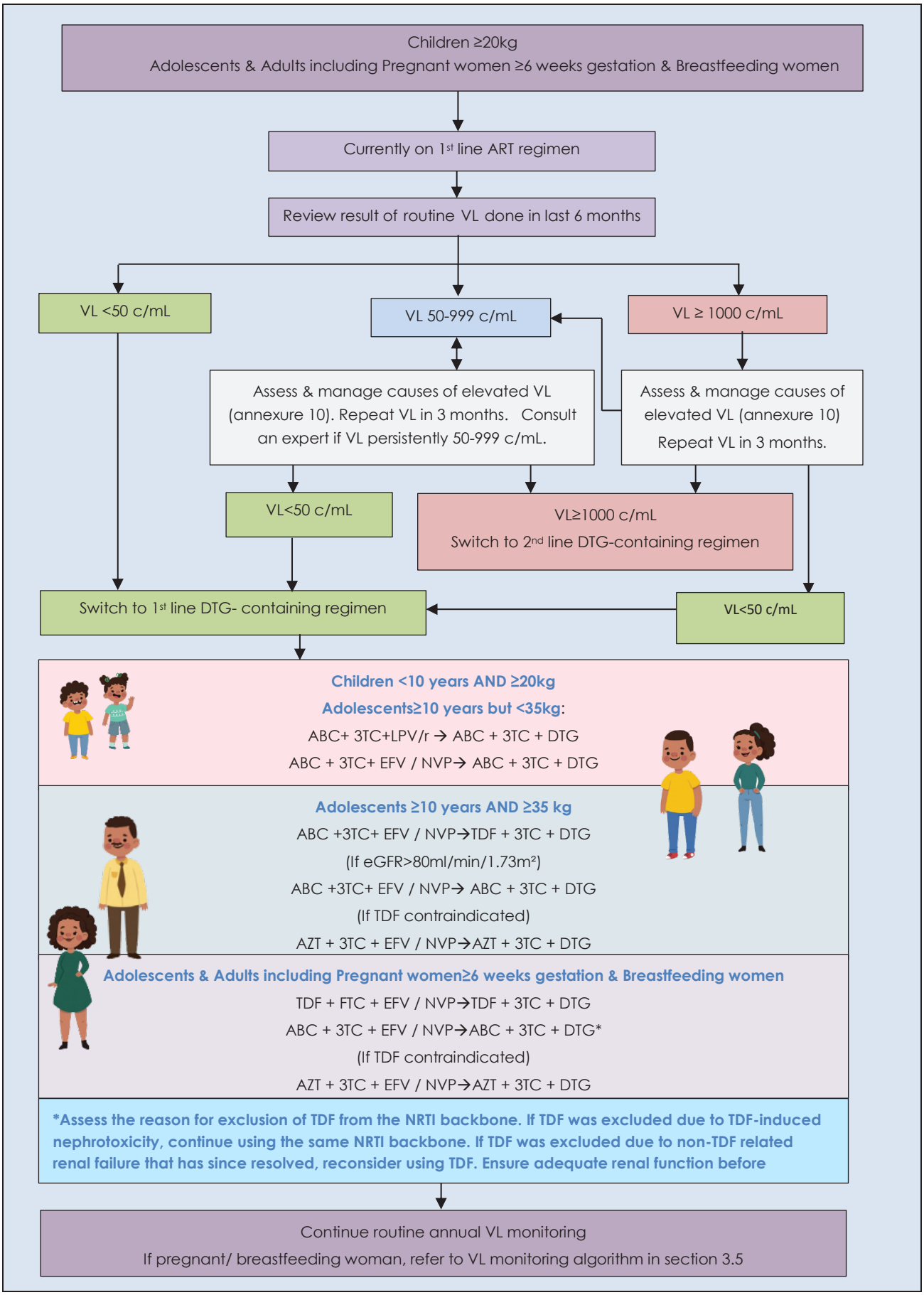
Box 2: Benefits & risks of using EFV

Benefits of using EFV	Risks of using EFV
Safe in pregnancy	Low genetic barrier to resistance
	Drug interactions with contraceptives
No significant interaction with TB treatment	Neuropsychiatric side-effects

2.5 Switching Stable ART-experienced Clients on 1st line regimens to DTG-containing regimens

- HIV-positive children ≥ 20kg, adolescents and adults including women who are pregnant ≥6 weeks gestation and breastfeeding women who are on 1st line ART regimens are eligible to be switched to a DTG-containing regimen if they have documented evidence of virological suppression (VL<50 c/mL) in the previous 6 months (figure 1). Use result of routine VL for assessment. No additional VL tests outside the routine schedule should be requested unless clinically indicated.
- Eligible clients should be offered the choice of switching to a new DTG-based regimen or remaining on their current EFV-based regimen- discuss benefits and risks of both options with the client (boxes 1& 2).
- The new regimen must include at least one fully active NRTI- review ART history.
- Patients with elevated viral loads must be assessed for the cause of an elevated VL and managed accordingly. See annexure 10.

Figure 1: Switching Stable Clients on ART to DTG-Containing regimens



3 ART IN PREGNANT AND BREASTFEEDING WOMEN

3.1 HIV Testing During Pregnancy and Breastfeeding

All newly diagnosed pregnant or breastfeeding clients with an unknown or previously negative HIV status must receive HIV Testing Services (HTS) on the same day that they present to the healthcare facility. If they present with their partners, they may be offered couples HTS as an option, but this should not delay same-day testing. Clients who are not known HIV positive and that are within one-year post-partum should be offered HTS as individuals or couples. If they test HIV positive, they should be initiated on ART according to adult guidelines.

Pregnant women who test HIV negative at the initial test must be offered repeat HIV testing at every antenatal appointment. It is essential that HIV testing is repeated at least at the following times:

- Around 20 weeks gestation (second trimester)
- Around 32 weeks gestation (third trimester)
- In labour/immediately after delivery
- At 6 weeks after delivery (EPI visit)
- Every 3 months while breastfeeding (ideally linked to contraceptive or baby wellness visits)

Explain and reinforce the importance of repeat testing at every visit. Clients should understand that retesting is done to detect seroconversion or new infection during pregnancy or breastfeeding, which carries a high risk of HIV transmission to the infant.

Pregnant women who present for antenatal booking in the third trimester must be managed carefully. A full antenatal assessment and HTS must be done on the same day if they have an unknown HIV status or have tested HIV negative previously. Known HIV positive clients on ART must have a viral load test done on the same day, and they must be given an appointment to return for the result within a week. Those who have interrupted treatment on ART must be counselled. They must be restarted on ART immediately. They should be referred to a medical officer if there are any other medical concerns, such as comorbid chronic conditions or opportunistic infections.

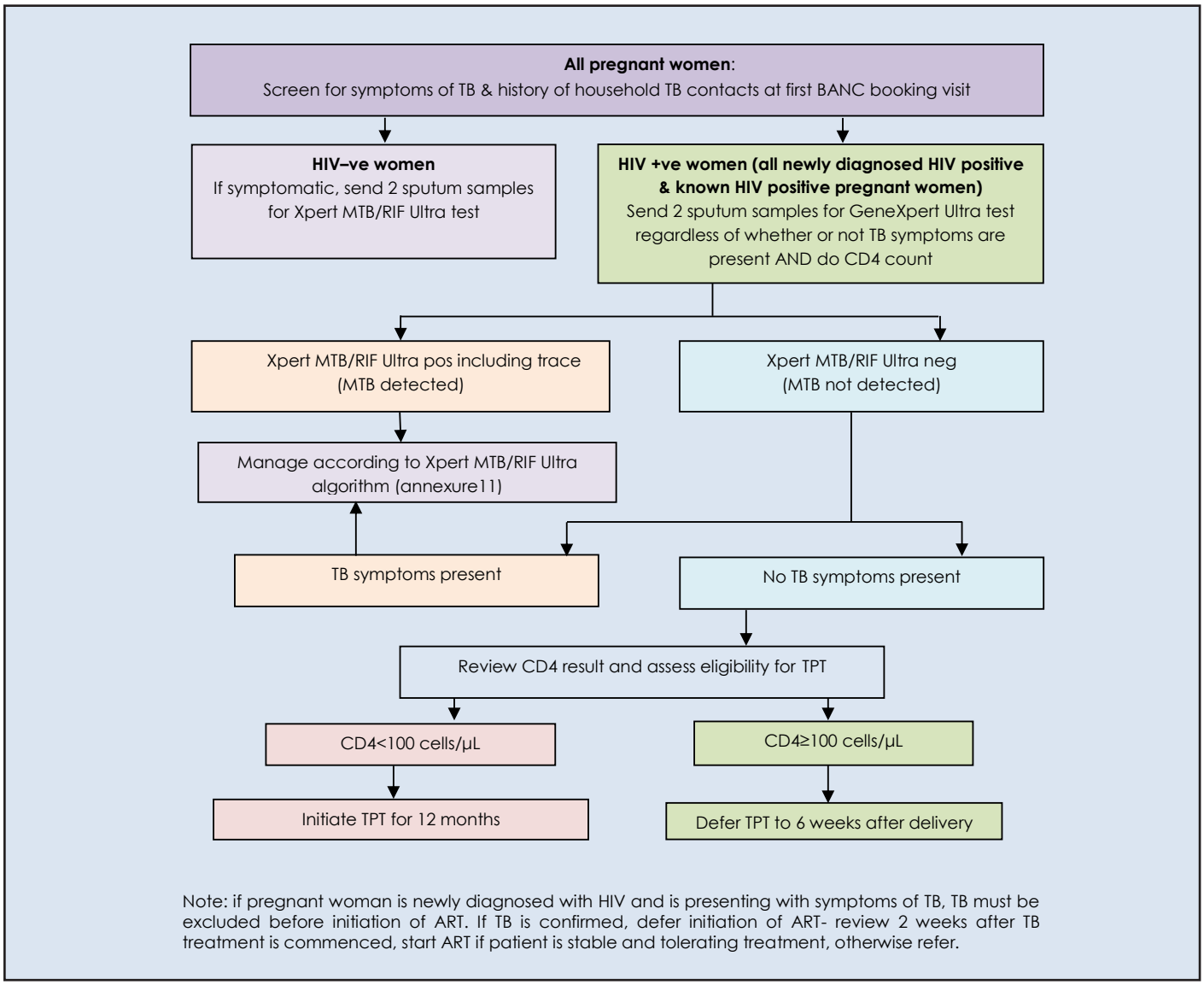
3.2 TB Symptom Screening, Universal Testing for TB & TPT During Pregnancy & Breastfeeding

All pregnant & breastfeeding women should be screened routinely for symptoms of TB at every visit. In addition, at the **first ANC booking visit**, all pregnant women who are newly diagnosed HIV positive or known HIV positive must be tested for TB using Gene-Expert Ultra sputum test **regardless of whether or not they have TB symptoms**. This is due to the lower sensitivity of the symptom screening test during pregnancy. Review results of GeneXpert Ultra after 2 days. If the client is newly diagnosed HIV positive and has symptoms of TB, defer ART until TB is excluded. If the client has no symptoms of TB, initiate ART on the same day (see figure 2).

Refer the client urgently to medical officer and consider admission if the client presents with TB symptoms and any of the following danger signs:

- Difficulty breathing
- Respiratory rate >30 breaths/min
- Temperature>38°C
- Pulse>100/min
- BP<90/60
- Coughing up blood
- Confusion, agitation or unable to walk unaided
- Weight loss >5%

Figure 2: TB Symptom screening, Universal Testing for TB & TPT at First BANC booking visit



If client is newly diagnosed HIV positive OR Known HIV positive but not on ART, and diagnosed with TB during pregnancy or breastfeeding:

- If TB is diagnosed after ART has been initiated/restarted, continue ART and start TB treatment.
- If client is on TLD, add DTG 50 mg daily if also on Rifampicin.
- Monitor for signs of developing IRIS.
- If TB is diagnosed before ART initiation/ restart, start TB treatment and defer initiation of ART- review 2 weeks after TB treatment is commenced and start ART if patient is stable and tolerating treatment, otherwise refer

If client is known HIV positive on ART and diagnosed with TB during pregnancy or breastfeeding:

- Review VL and continue ART
- If TB is excluded, the client is eligible for TPT for 12 months. Initiate TPT during pregnancy only if CD4<100 cell/uL. If CD4≥100 cell/uL, defer TPT to 6 weeks after delivery.
- Refer client to CBS

3.3 Screening & Management of Syphilis During Pregnancy & Breastfeeding

Syphilis is a sexually transmitted infection (STI) that can have multiple different presentations but can also be asymptomatic. The signs of secondary syphilis occur 6-8 weeks after the primary ulcer (chancre) and include a generalized rash including palms and soles). Flu-like symptoms, flat wart-like genital lesions (condylomata lata), mouth ulcers and patchy hair loss. Tertiary syphilis occurs many years later, and may affect skin, bone, heart and nervous system. Transmission of syphilis to infants occurs in 40% of mothers with untreated syphilis.

Screen all pregnant women for clinical signs of syphilis & other STIs **and** test for syphilis infection at the first antenatal visit. If the test is positive, confirm with an appropriate confirmatory test (see table 2) If the test is done before 20 weeks gestation, and is negative, repeat at 32 weeks. If syphilis infection is confirmed at any stage, treat with **benzathine penicillin 2.4MU intramusularly weekly for 3 weeks** (reconstitute with 6mL lidocaine without epinephrine). If woman is penicillin sensitive, refer for penicillin desensitization. If initial RPR titre >1:8, repeat RPR 3 months after last injection to confirm fourfold reduction in RPR titres.

Table 2: Initial & Confirmatory tests for Syphilis

First test	Confirmatory test
RPR (rapid or laboratory)	TPHA (laboratory)
TPHA (HIV-syphilis combination or stand-alone test)	RPR (rapid or laboratory)

3.4 Initiation of ART During Pregnancy and Breastfeeding

All newly diagnosed HIV-positive pregnant or breastfeeding women must be initiated on ART on the same day (if ART service available, no suspicion of TB and patient readiness has been confirmed) in order to minimise the risk of transmission of HIV to their infants. Known HIV-positive women who are not yet on ART must also be initiated at the first visit. They must receive post-test counselling with support for disclosure to a supportive partner, family member or friend, followed by a session of pre-ART and adherence counselling.

The management of pregnant or breastfeeding women eligible for ART is summarised in table3. Refer all unbooked pregnant clients for antenatal booking as soon as possible. Infants of breastfeeding mothers must be clinically assessed for signs of HIV or HIV-related infection and referred for HIV testing and Post- Exposure Prophylaxis (PEP) (section 3). Clients must be seen 1 week after initiating ART in order to review blood results, enquire about side-effects and provide adherence support. Confirm that the pregnant client has booked for antenatal care and record starting date of ART and treatment regimen in antenatal booklet if possible and refer to CBS.

All clients who have tested HIV-negative during pregnancy or are not known to be HIV-positive must be tested for HIV during labour or at delivery, so that HIV prophylaxis can be given and lifelong ART initiated (box 3).

Box 3: Management of clients testing HIV-positive during Labour or at Delivery

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 the necessary information on DTG and EFV-based regimens including the risk of NTDs, and enable to make an informed choice. Provide her with a choice of contraceptive options as desired. Appropriate ART literacy neducation should be given to the woman before she leaves the facility.

Table 3: Management of pregnant or breastfeeding clients who are newly diagnosed HIV-positive or known HIV- positive but not on ART

On Same Day as HIV Positive Diagnosis	At Follow-up Visit Within 1 week
HIV and pre-ART counselling	HIV and ART counselling
Adherence counselling	Adherence counselling
CD4 count	Review CD4 results: If CD4<100 cells/mL, check reflex CrAg result. If positive, refer on same day for lumbar puncture If pregnant, assess eligibility for TPT (see below) If CD4≥200 cells/mL and WHO clinical stage 1 and no TB, stop Cotrimoxazole prophylaxis (see section 8)
Serum Creatinine + enquire about history of renal disease	Review Creatinine results
WHO staging	Confirm WHO staging and need for cotrimoxazole prophylaxis
TB symptom screening & enquire about TB contacts. Send 2 sputum samples for TB GeneXpert Ultra test regardless of whether symptoms of TB are present. If symptomatic or history of close TB contact, delay initiation of ART and follow up for TB GeneXpert Ultra result after 2 days.	Review results of sputum TB GeneXpert test. If TB GeneXpert pos initiate TB treatment. Start ART after 2 weeks, when TB symptoms improving and client is tolerating TB treatment. If ART already started, continue with regimen. If on DTG- containing regimen, give additional dose of DTG 50mg 12 hours after daily dose of ART if on Rifampicin. If TB GeneXpert neg but TB symptoms present, refer to medical officer for assessment and decision on whether to start TB treatment. Follow up for culture result after 1 month. If TB GeneXpert neg and diagnosis of TB excluded, initiate ART.
TPT: If pregnant and no clinical suspicion of TB, defer TPT until CD4 result available. If breastfeeding and no clinical suspicion of TB , start TPT if no contraindications (no need to give TPT if patient recently completed TB treatment or full course of TPT)	TPT: If pregnant and CD4<100 cells/uL, CrAg neg, Xpert neg, & no clinical suspicion of TB , start TPT if no contraindications (no need to give TPT if patient recently completed TB treatment or full course of TPT) If pregnant and CD4≥100 cells/uL and no clinical suspicion of TB, defer TPT until 6 weeks after delivery
RPR and STI screening	STI screening, review RPR result. Treat if necessary.
Hb	Review Hb result.
Screen for chronic diseases-check BP, and urine dipstix for protein and glucose.	
If no TB symptoms initiate/ restart ART on same day. ART-naïve clients: If no history of renal impairment AND ≥ 6 weeks pregnant: Initiate ART with Tenofovir +Lamivudine + Dolutegravir (TLD) as fixed dose combination If history of renal impairment AND ≥ 6 weeks pregnant: Initiate ART with Abacavir + Lamivudine + Dolutegravir ART-experienced clients currently not on ART + ≥6 weeks pregnant: If previously on 1st regimen (TEE) with VL<50c/mL, restart ART with TLD If client chooses to restart TEE, do baseline VL. If previously on 1st regimen TEE with VL≥50c/mL or unknown VL, restart ART with Zidovudine + Lamivudine + Dolutegravir (ALD). If Hb<8g/dL, avoid Zidovudine – restart ART with Tenofovir +Lamivudine + Lopinavir/r If previously on 2nd or 3rd line regimen, restart the same regimen	If Serum Creatinine ≥85mmol/l (if pregnant) or CrCl <60ml/min (if breastfeeding): Avoid Tenofovir, substitute with Abacavir Monitor for side-effects and provide reassurance, adherence support and advice.
If no ART service available, start Zidovudine 300mg every 12 hours in pregnant women if Hb>8g/dL and refer to ART site urgently. If breastfeeding, do not give Zidovudine and refer to ART site urgently.	
Give Cotrimoxazole prophylaxis (CPT) - refer to section 8. If breastfeeding, provide infant post-exposure prophylaxis (table 5). Refer to CBS.	

3.5 Viral Load Monitoring of Pregnant and Breastfeeding Women on ART

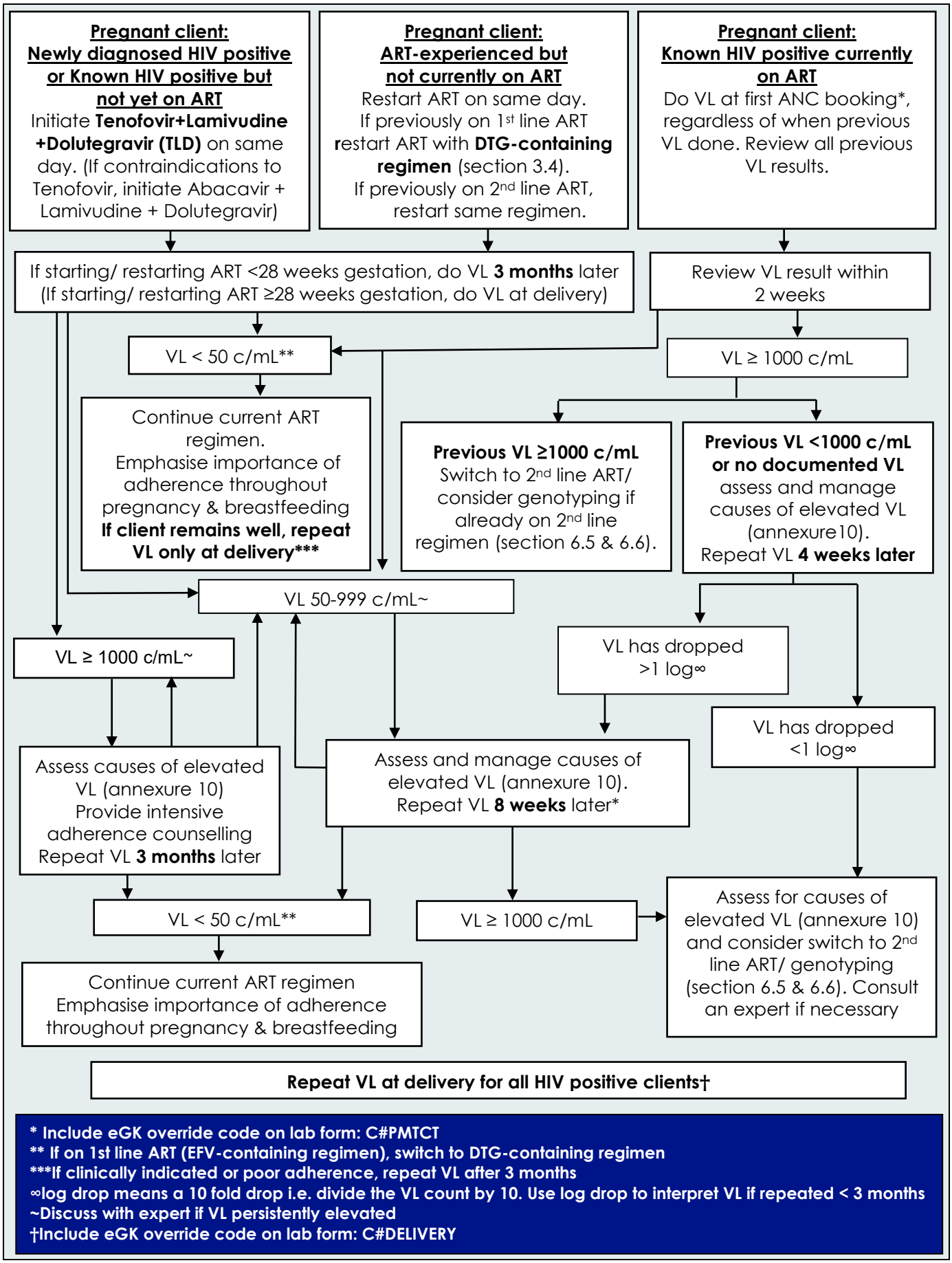
Monitoring of Viral load (VL) is required in order to assess the risk of HIV transmission to infants. Ensure that clients understand the purpose of regular VL monitoring. HIV transmission to infants is more likely to occur in clients who are newly initiated or restarted on ART late in pregnancy, and clients who are on ART with VL≥1000 during pregnancy. These clients should be discussed with an experienced clinician. Provide adherence support and counselling to all pregnant clients at every BANC visit and emphasise the importance of adherence throughout the pregnancy and during breastfeeding. Algorithms for VL monitoring and management of unsuppressed VL's in pregnant and breastfeeding women are illustrated below in figure 3 and 4. Women with VL ≥50 copies/mL, should be managed by a medical officer.

Monitor safety blood tests according to standard adult recommendations (refer to section 5.6).
Repeat VL at delivery for all HIV positive women. This result must be reviewed at the post-natal visit within a week after delivery (see section 4.1.2). Women with elevated viral loads must have a thorough assessment of the cause of the elevated VL. See annexure 10.

Repeat VL 6 months after delivery for all HIV positive women, regardless of infant feeding method- align with well child visit. Thereafter, repeat VL 6 monthly if breastfeeding, until breastfeeding is stopped. If VL >1000 at any stage, restart infant post-exposure prophylaxis (see table 5).

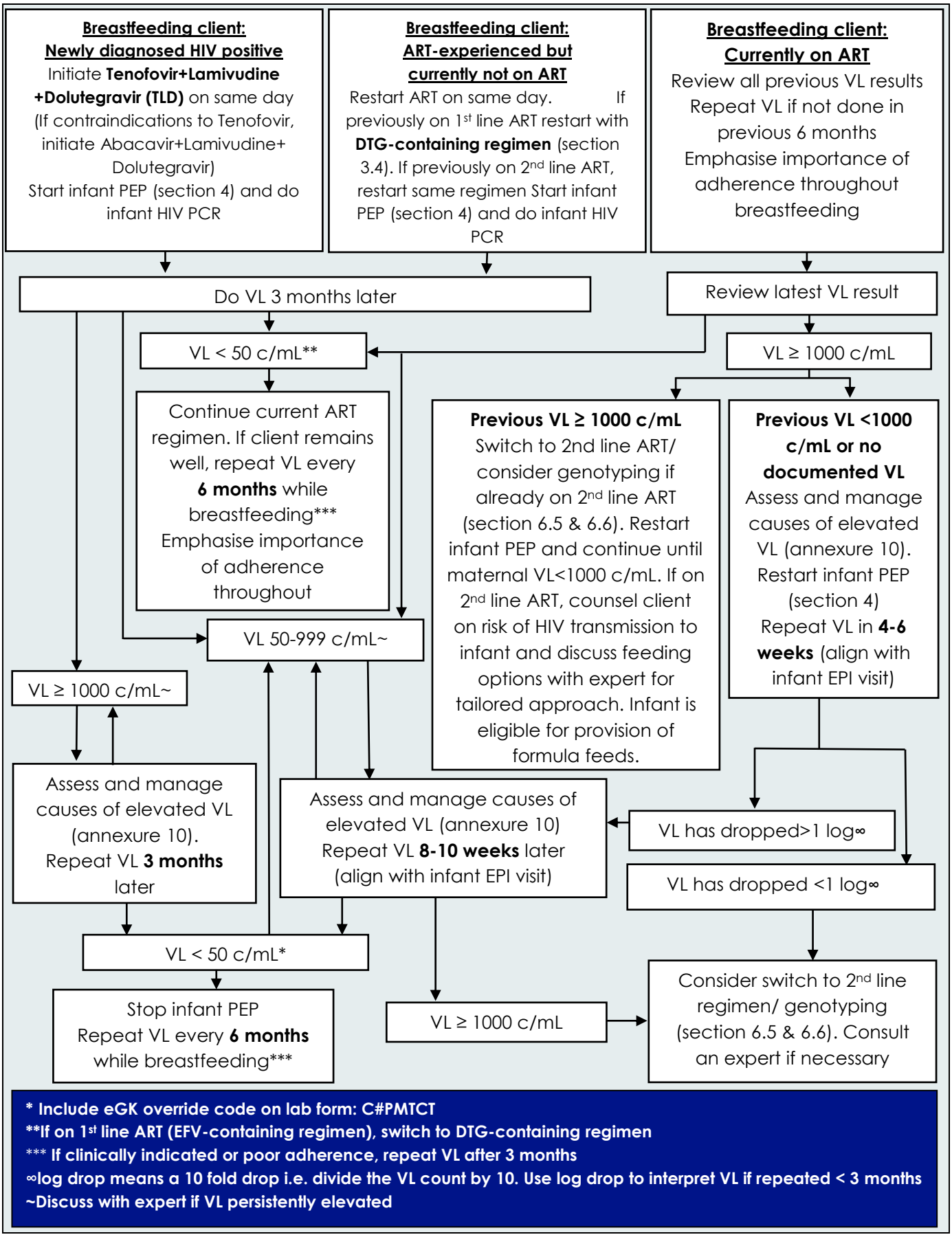
3.5.1 Viral Load Monitoring During Pregnancy

Figure 3: Viral load monitoring during pregnancy



3.5.2 Viral Load Monitoring During Breastfeeding

Figure 4: Viral load monitoring during breastfeeding



4. CARE OF THE INFANT EXPOSED TO HIV, TB OR SYPHILIS

4.1 CARE OF THE HIV-EXPOSED INFANT

Mothers should also be intensively counselled about the importance of long-term adherence to ART and all HIV infected mothers and their babies referred to CBS for ART adherence and infant feeding support.

4.1.1 HIV Testing in HIV-exposed Infants

Infants of HIV-infected mothers may be at risk of acquiring HIV during pregnancy, and delivery process and during breastfeeding. HIV testing during and after the period of exposure is necessary to diagnose HIV infection early and initiate ART. HIV counselling and consent is always required from parents or primary caregivers of infants before HIV testing can be done. Any child under 2 years with a positive HIV PCR or Rapid/ ELISA test should have their HIV status confirmed with a HIV PCR test on a new sample.

Table 4: HIV testing in HIV-exposed infants

Time of HIV test	Who should be tested	Which test should be used
At birth (within 48h)	All HIV-exposed infants Abandoned newborns/ orphans (HIV-exposure confirmed with Rapid Determine ® test	HIV PCR test If positive, confirm with a 2nd HIV PCR test
At 10 weeks	All HIV-exposed infants not on ART (irrespective of feeding choice)	HIV PCR test If positive, confirm with a 2nd HIV PCR test
At 6 months	All HIV-exposed infants not on ART (irrespective of feeding choice) **Infants not known to be HIV-exposed:** • At six months of age, establish the HIV status of all infants not already known to be HIV-exposed • Offer an HIV test to the mother. If she tests HIV negative, no infant test is required • If the mother is not available, or refuses an HIV test, do an HIV rapid test on the infant • All positive infant rapid tests need to be confirmed with an HIV-PCR.	HIV PCR test If positive, confirm with a 2nd HIV PCR test
Around 18 months (Universal HIV testing)	All infants regardless of HIV exposure at birth except those on ART	Rapid HIV antibody screening test If result is positive, confirm with HIV PCR test If result is indeterminate, do HIV PCR test. If the PCR test is positive, confirm with a 2nd HIV PCR test
At any time	**All infants with:** • Mothers who are newly diagnosed HIV positive while breastfeeding • Clinical features suggestive of HIV infection • Acute, severe illness • IMCI classification of Suspected symptomatic HIV infection • IMCI classification of Possible HIV infection • TB diagnosis or history of TB treatment • Risk of sexual assault • Wet-nursed or breastfed by a woman with unknown or HIV-positive status • Abandoned children or adoption **Family and social history:** • Parental request to test the child • Father or sibling with HIV infection • Testing of all siblings if mother diagnosed HIV positive • Death of mother, father or sibling • When the mother's HIV status is unknown	Test depends on the infant's age: <18 months HIV PCR test If positive, confirm with a 2nd HIV PCR test 18 months to 2 years Rapid HIV antibody screening test. If positive, confirm with a HIV PCR test ≥ 2 years Rapid HIV antibody screening test If positive, confirm with rapid HIV antibody confirmatory test If results are indeterminate, do HIV ELISA test For abandoned children and children considered for fostering or adoption: Confirm maternal HIV exposure with rapid HIV test AND do infant HIV PCR test
6 weeks after final breastfeed	All HIV-exposed infants who were breastfed	Do age appropriate HIV test as above

4.1.2 Post-Exposure Prophylaxis (PEP) in HIV-Exposed Infants

All HIV exposed infants should receive post- exposure prophylaxis with **nevirapine (NVP) + zidovudine (AZT)** post-delivery (refer to dosing tables 6, 7 & 8). The risk of HIV transmission from HIV positive mother to infant should be classified as high or low according to the result of the VL done **at delivery**. This result will most likely not be available when the mother and infant are discharged, therefore must be reviewed at the **routine post-natal visit (day 3-6)**. Parents and primary care-givers of infants must be counselled about the role of ARVs in preventing transmission of HIV. Administration of medication to infants should be demonstrated, and the importance of giving it every day for the duration specified should be emphasized. They should be encouraged to return for assistance if any side effects or problems administering medication are experienced. All HIV-exposed infants should be issued with a minimum of 6 weeks PEP supply of NVP + AZT, which they must bring to the post-natal visit. Once the delivery VL has been reviewed, continue PEP according to the risk classification in table 5. If the risk is low (VL<1000), stop the AZT and **return unused AZT to the pharmacy to discard.**

Table 5: Post-exposure prophylaxis (PEP) in HIV-exposed infants

Subgroup of HIV-exposed infants	ARVs for Post-exposure Prophylaxis (PEP)
1. Low risk of HIV transmission at birth: Mother on ART with documented VL <1000 copies/mL at delivery	**Nevirapine daily for 6 weeks** *(regardless of feeding choice)* Do HIV PCR at birth or at first presentation to facility. If positive, do confirmatory PCR and transition to ART. If negative, repeat PCR at 10 weeks and 6 weeks after final breastfeed, 6 months & 18 months.
2. High risk of HIV transmission at birth: Mother on ART with VL ≥1000 copies/mL at delivery **OR** Unknown maternal HIV status or abandoned /orphaned infant (exposure confirmed with rapid HIV antibody test)	**If breastfeeding:** **Nevirapine daily for at least 12 weeks** **+** **Zidovudine twice daily for 6 weeks** *(Only stop NVP once maternal VL <1000 copies/mL)* **If formula feeding:** **Nevirapine daily for 6 weeks** **+** **Zidovudine twice daily for 6 weeks** Do HIV PCR* at birth or at first presentation to facility. If positive, do confirmatory PCR and transition to ART. If negative, repeat HIV testing at 10 weeks, 6 weeks after final breastfeed, 6 months & 18 months.
3. Increased risk of HIV transmission during breastfeeding Mother on ART with most recent VL≥1000 copies/mL **OR** Mother HIV positive but not on ART: o Newly diagnosed HIV-positive while breastfeeding o Previously diagnosed HIV-positive but not initiated on ART or discontinued ART	**Nevirapine daily for at least 12 weeks** **+** **Zidovudine twice daily for 6 weeks** *(Only stop NVP once maternal VL <1000 c/mL. Assess & manage causes of unsuppressed VL (annexure10). If failing 1st line ART, repeat VL after 3 months. Switch to 2nd line ART if VL still >1000 c/mL (section 6.5). If failing 2nd line ART, consider genotyping (section 6.6). Counsel client on risk of HIV transmission to infant and discuss feeding options with expert for tailored approach. Infant is eligible for provision of formula feeds)* Start Cotrimoxazole prophylaxis if infant ≥4 weeks old. Do HIV PCR*. If positive, do confirmatory PCR and transition to ART. If negative, repeat HIV testing at, 6 weeks after final breastfeed, 6 months &18 months.

*If result indeterminate, refer to Annexure 12 for further management.

- Administer the first dose of oral PEP to the newborn as soon as possible after birth (preferably within 1 hour of birth) (refer to table 7 & 8 for dosing).
- Neonates who are nil per mouth (NPO) e.g. Necrotizing Enterocolitis (NEC), intestinal anomaly/ obstruction should receive intravenous Zidovudine (AZT) until oral feeding and PEP is tolerated (refer to table 6).
- At discharge, provide PEP for the first 6 weeks and advise mothers that they will receive more Nevirapine (NVP) at the next visit.
- Infants who have suspected AZT-related anaemia/ neutropaenia from prolonged foetal (in utero) exposure to AZT should be referred for investigation and further management.
- Infants who do not tolerate NVP or develop NVP toxicity should be switched to oral AZT for 4 weeks. Additional measures (optimised maternal ART/heat treatment of breast milk) may be required for prophylaxis during breastfeeding- consult an expert.
- Certain babies are at higher risk of developing anaemia on zidovudine e.g. premature and malnourished infants. Close monitoring is recommended and if in doubt discuss with an expert and refer as needed.
- Transition infants who test HIV positive at birth from PEP to ART (refer to annexure 3).
- Fast track infants who test HIV positive at a later stage for ART (refer to section 5)

Table 6: Intravenous dosing of Zidovudine for PEP in HIV-exposed infants

Intravenous Zidovudine (AZT) (10 mg/mL in 200mg vial)		
Not a multi-dose vial. Prepare in sterile pharmacy for multiple doses	**Age**	**IVI Dose**
	≥35 weeks gestation	1.5 mg/kg/dose 6 hourly
	<35 weeks gestation	1.5 mg/kg/dose 12 hourly
	Once full enteral feeds are tolerated, resume oral NVP. At discharge, provide NVP.	

Table 7: Oral dosing of Zidovudine for PEP in HIV-exposed infants

Zidovudine (AZT) syrup (10mg/ml)		
Age	**Current weight**	**Twice daily dose**
Premature infants <35 weeks of gestational age at birth	Birth – 2 weeks of age	2 mg/kg/dose (0.2 ml/kg/dose) 12 hourly
	2 weeks – 6 weeks of age	3 mg/kg/dose (0.3 ml/kg/dose) 12 hourly
Birth to 6 weeks (infants ≥35 weeks of gestation)	<2 kg, ≥35 weeks gestation	4mg/kg/dose 12 hourly
	2.0-2.49kg	1ml (10mg) 12 hourly
	>2.5kg	1.5ml (15mg) 12 hourly
>6 weeks (doses according to ART Dosing Chart for Children)	<3kg	4mg/kg/dose 12 hourly (0.4ml/kg/dose 12 hourly)
	3.0–5.9kg	6ml (60mg) 12 hourly
	6-7.9kg	9ml 12 hourly
	8-13.9kg	12ml 12 hourly

Table 8: Oral dosing of Nevirapine for PEP in HIV-exposed infants

Nevirapine (NVP) syrup (10mg/mL)			
Age	**Current weight**	**Once daily dose**	
Birth to 6 weeks	*< 2.0kg	Birth to 2 weeks	2mg/kg/dose (0.2mL/kg/dose) daily
		2 – 6 weeks	4mg/kg/dose (0.4mL/kg/dose) daily
	2.0-2.49kg	1mL (10mg) daily	
	>2.5kg	1.5mL (15mg) daily	
6 weeks to 6 months	Any	2mL (20mg) daily	
6 to 9 months	Any	3mL (30mg) daily	
9 months until 4 week after all breastfeeding has stopped	Any	4mL (40mg) daily	

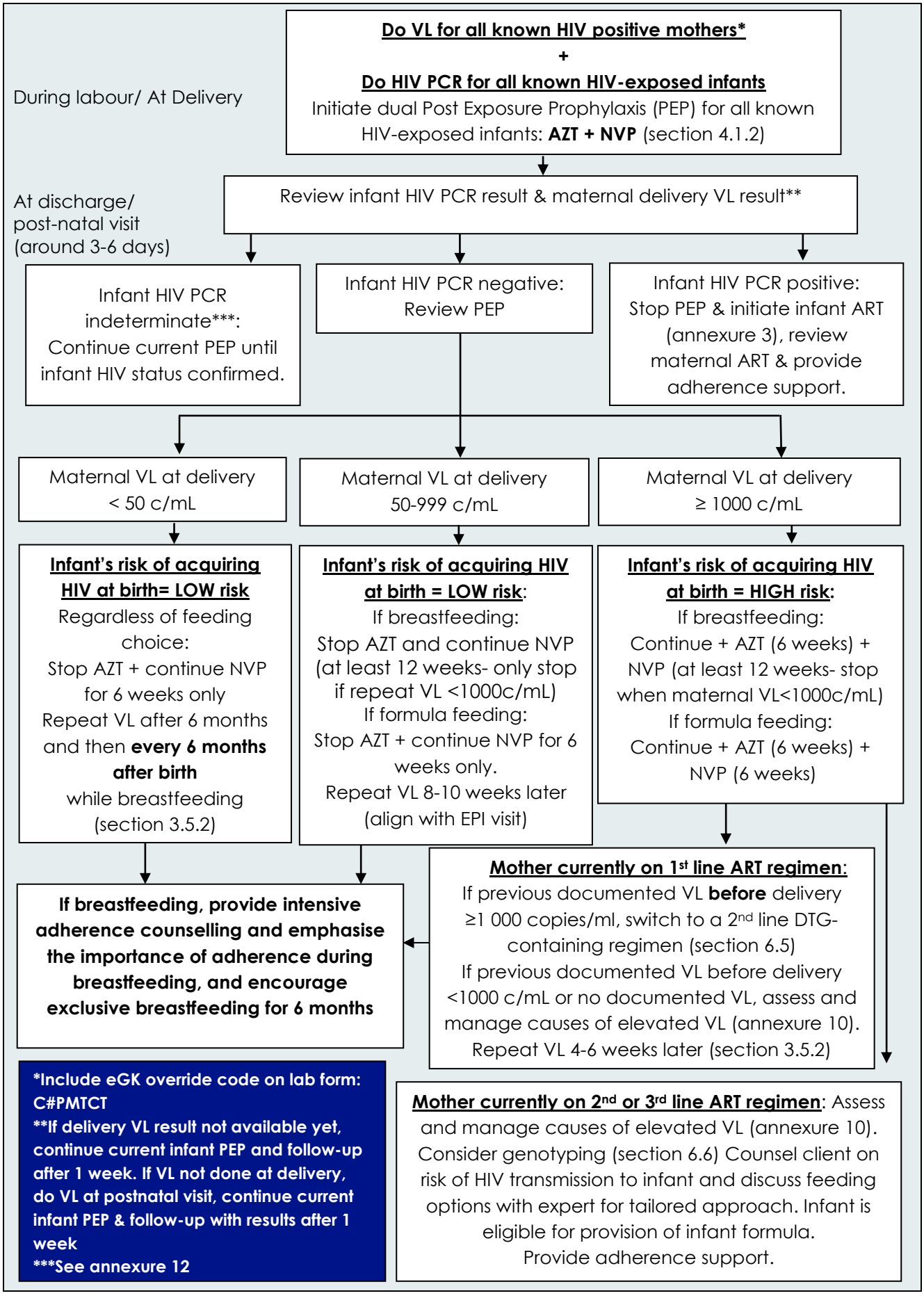
*Premature infants < 35 weeks gestational age should be dosed using expert guidance.
if the infant still weighs <2 kg at 6 weeks of age, continue with dosage of 4 mg/kg/dose (0.4 ml/kg/dose) once daily until reaches 2 kg

Table 9: Oral dosing of cotrimoxazole for PEP in HIV-exposed infants

Cotrimoxazole syrup (200/40mg/5mL)	
Current weight	**Once daily dose**
2.5 to < 5kg	2.5mL
5 to <14kg	5mL
Stop cotrimoxazole when PCR is negative ≥6 weeks after full cessation of breastfeeding AND infant is clinically HIV negative	

4.1.3 Management of Infant PCR and Maternal VL Result at Post-Natal Visit

Figure 5: Review of Infant PCR and Maternal VL Results



4.1.4 Infant feeding

All pregnant women (HIV-positive, HIV-negative or with unknown HIV status) should receive at least four antenatal counselling sessions on infant feeding. Please refer to Circular H166/2012: Infant feeding counselling guideline for detailed information on the stepwise approach for infant feeding counselling.

Counsel and support mothers known to be HIV infected to exclusively breastfeed their infants for six months and continue breastfeeding until **24 months** of age, with appropriate complementary feeding whilst taking antiretroviral treatment as prescribed. ART reduces the risk of postnatal HIV transmission in the context of mixed feeding. Although exclusive breastfeeding is recommended, practicing mixed feeding is not a reason to stop breastfeeding if the mother is on ART. Mothers living with HIV and healthcare workers can be reassured that shorter duration of breastfeeding is better than never initiating breastfeeding at all.

The most important benefit of exclusive breastfeeding is the reduction in the risk of HIV transmission and improved child survival. Mothers must be counselled about the risks of mixed feeding including the risk of gastroenteritis associated with the use of bottles, teats and pacifiers to their infants during their first six months of life.

Mothers should also be intensively counselled about the importance of long-term adherence to ART and all HIV infected mums and their babies referred to CBS for ART adherence and infant feeding support. Please refer to Circular H118/2017. All HIV-exposed infants must be provided with prophylactic NVP alone or in combination with AZT where applicable. Infants who are growth faltering or are at high risk of poor growth should be referred for appropriate nutritional care and support.

HIV-positive mothers who decide not to breastfeed their infants (after appropriate counselling and education) should understand that formula is not routinely provided as part of the PMTCT programme. Counsel these mothers on appropriate exclusive formula feeding in amount and frequency, safe preparation, storage and feeding mechanism, including a back demonstration to confirm that they understand how to safely prepare and feed infant formula. They should be able to provide adequate formula for their infants as a replacement feed to their HIV uninfected infants when specific conditions are met:

Box 4: Conditions for replacement infant feeding

1. Safe water and sanitation are assured at the household level and in the community, and
2. The mother or other caregiver can reliably provide sufficient infant formula to support normal growth and development of the infant, and
3. The mother or caregiver can prepare it cleanly and frequently enough so that it is safe and carries a low risk of diarrhea and malnutrition, and
4. The mother or caregiver can, in the first six months, exclusively give infant formula, and
5. The family is supportive of this practice, and
6. The mother or caregiver can access health care that offers comprehensive child health services.

The only approved HIV-related medical condition (National Department of Health) where infant formula may still be provided is when a mother has been on second or third-line ART for at least 3 months and has a viral load above 1000 copies/mL. Mothers who are too ill to breastfeed (e.g. MDR TB) will also be provided with infant formula.

If an infant test HIV-positive, encourage breastfeeding for 2 years and longer as extended breastfeeding is better for an HIV-infected infant's health, nutrition and survival. Emphasize the importance of continuing infant and maternal ART and monitoring viral loads regularly. Remind mothers that growth monitoring enables early intervention and it is very important to record weight of child monthly in the first two years of life and three-monthly thereafter until they turn 5 years old.

All healthcare providers caring for mothers, infants, and young children should fully adhere with all the provisions of the South African Regulations Relating to Foodstuffs for Infants and Young Children (R 991).

4.2 CARE OF THE TB-EXPOSED INFANT

Identify the infant at risk of acquiring TB:

- Mother diagnosed with new episode of TB in last 2 months of pregnancy
- Mother on TB treatment during pregnancy with poor response to TB treatment or still smear positive at delivery
- Mother with clinical signs & symptoms of TB during pregnancy but not investigated prior to delivery, TB diagnosed after delivery

Do thorough clinical examination of infant:

- If asymptomatic, eligible for TB Preventive Therapy (TPT)
  - Start INH 10mg/kg/day for 6 months (for dosing see section 8-table 21)
  - **Do not give BCG at birth**
  - Follow up at every contact session- assess adherence to TPT
  - Test for HIV as per routine schedule & treat if relevant
  - If HIV neg, give BCG 2 weeks after TPT complete
  - If HIV pos, give BCG if on ART 2 weeks after TPT is complete. If ART initiation is delayed due to clinical complications, discuss with expert.

- If symptomatic: resp rate >60/min, difficulty breathing, feeding problems, poor weight gain, abdominal distension, enlarged liver/spleen, jaundice- refer to hospital for investigation
  - **Do not give BCG at birth**
  - If no TB diagnosed, eligible for TPT- manage as above (asymptomatic infant)
  - If TB diagnosed, continue treatment as initiated in hospital (regimen 3)
  - Test for HIV as per routine schedule & treat if relevant
  - If HIV neg, give BCG 2 weeks after TB treatment complete
  - If HIV pos, give BCG if on ART 2 weeks after TB treatment is complete. If ART initiation is delayed due to clinical complications, discuss with expert.

4.3 CARE OF THE SYPHILIS-EXPOSED INFANT

Identify the infant at risk of acquiring syphilis:

- Mother tested positive for syphilis during pregnancy

Do thorough clinical examination of infant:

- If asymptomatic, treat baby with Benzathine penicillin 50 000u/kg intramuscularly (IM)stat only if-
  - Mother was not treated, or
  - Mother has received less than 3 doses of Benzathine penicillin, or
  - Mother delivers within 4 weeks of commencing treatment
- If symptomatic-signs include desquamative rash (red/blue spots or bruising especially on soles and palms), jaundice, pallor, distended abdomen due to enlarged liver or spleen, low birthweight, respiratory distress, large pale placenta, hypoglycaemia
  - Refer all symptomatic babies for treatment of congenital syphilis
  - Procaine penicillin 50 000u/kg IM daily for 10 days, or Benzyl penicillin (penicillin G) 50 000u/kg/dose 12 hourly intravenously (IV) for 10 days
  - Erythromycin does not reliably cure syphilis in either the mother or baby

5. ART IN INFANTS & CHILDREN

5.1 Criteria and Timing of Initiation of ART

Eligibility criteria for initiating ART in infants, children and early adolescents who are newly diagnosed with HIV are shown in box 4. Those who are eligible should have neurodevelopmental, nutritional and clinical assessments, TB screening and HIV clinical staging before initiating ART. Caregivers must receive counselling on how to administer medication, monitor side-effects and deal with challenges to adherence. Eligible children should be started on ART as soon as possible. Patients may be fast-tracked for ART under certain circumstances (refer to box 4). **Infants < 2 years of age who are newly diagnosed as HIV positive are eligible for genotype resistance testing if their mothers were exposed to PI-based ART during pregnancy or breastfeeding.**

Box 5: Eligibility criteria for ART and fast-tracking of ART

Eligibility for starting ART
• All HIV- positive children irrespective of CD4 or clinical staging
Patients requiring fast tracking (i.e. start ART within 7 days)
• Infants • Children < 5 years of age • WHO clinical Stage 4 • MDR or XDR-TB • CD4 count ≤200 cells/µl or ≤15%

5.2 Monitoring of Infants & Children on ART

Table 10: Monitoring of infants, children and early adolescents on ART

At initial Diagnosis of HIV – baseline clinical evaluation	Purpose
Confirm HIV status	Ensure that NDoH HIV testing algorithm has been followed
Genotype resistance test: Infants < 2 years of age who are newly diagnosed as HIV positive if their mothers were exposed to PI-based ART during pregnancy or breastfeeding	To screen for resistance to PI
Document weight, height, head circumference (<2yrs) and development	To monitor growth , development and to identify moderate and severe malnutrition; identify eligibility for ART
Screen for TB symptoms or contacts	To identify TB/HIV co-infection & eligibility for TPT
TB GeneXpert	Only for those with a positive TB symptom screen
WHO Clinical Staging	To determine urgency and timing of ART initiation
CD4 count/%	Children < 5 years: DO NOT wait for CD4 count to start ART
	To determine eligibility for Cotrimoxazole Preventive Therapy (CPT) (refer to section 8)
BC + differential WCC	To detect anaemia; neutropaenia; thrombocytopaenia
Neurocognitive developmental assessments	To identify children with neurodevelopmental delay. Use appropriate available tool (refer to annexure 2)
ALT (if jaundiced or on TB treatment)	To assess for liver dysfunction
On ART	**Purpose**
Height, weight, head circumference (<2yrs) and development	To monitor growth and developmental stages; adjust ARV dosages according to weight
Clinical assessment and WHO staging	To monitor response to ART and manage side effects and CPT eligibility
CD4: All at month 12 Then: Repeat CD4 every 6 months until meet criteria to discontinue CPT If at any later stage VL ≥1000 c/mL on 2 consecutive tests, repeat CD4 every 6 months to monitor for immunological failure Restart CPT if indicated.	To monitor susceptibility to opportunistic infections and eligibility for Cotrimoxazole Preventive Therapy (CPT) [Refer to section 8]
VL: All at month 4 and 12 Then If VL<50 copies/mL, repeat every 12 months. If VL ≥50 copies/mL, address adherence, repeat after 3 months	To monitor virological response to ART To identify treatment failure and problems with adherence Obtain expert advice if persistent viraemia of VL between 50 and 999
Hb and differential WCC at month 1, 3 and 6 months if on AZT	To identify AZT-related anaemia and neutropenia
Total Cholesterol + Triglycerides at month 3 (non-fasting) if on a PI	To monitor for PI-related metabolic side-effects If above acceptable range, obtain expert advice. Refer if TG > 10. Consider switch to Atazanavir/r if >6 years old and ≥ 15kg
Neurocognitive developmental assessments	With appropriate available tool (refer to annexure 2)

*Refer to Annexure 5 & 6 for standard drug dosages. Refer to Annexure 11 for reporting of adverse drug reactions

5.3 Standard ART regimens for Infants & Children

Table 11: Standard ART regimens for infants & children

1st Line Regimens*	
Neonates (infants <4 weeks old) and >2.5kg	Zidovudine + Lamivudine + Nevirapine Review at 1 month and if >3kg switch to Abacavir + Lamivudine + Lopinavir / ritonavir Refer to Annexure 3 for initiation of ART in infants ≤4 weeks old. Consult an expert for advice if necessary.
All infants ≥ 4 weeks old and ≥ 42 weeks gestational age and children <20kg	Abacavir + Lamivudine + Lopinavir/Ritonavir
Children 20-35 kg or <10 years old	Abacavir + Lamivudine + Dolutegravir
Adolescents ≥35 kg AND ≥10 years old	Transition to Adult & Adolescent regimens (refer to section 5.4) Tenofovir + Lamivudine + Dolutegravir Ensure adequate renal function If Tenofovir contraindicated: Abacavir + Lamivudine + Dolutegravir
Adverse effects related to Lopinavir/ritonavir Hyperlipidaemia Severe gastrointestinal side effects > 6 weeks Simplification to a once daily regimen	From 6 years and ≥ 15kg: Switch Lopinavir/ ritonavir to Atazanavir/ ritonavir
2nd Line Regimen* Failed 1st line NNRTI based Regimen	
1st line NNRTI-based regimen:	Recommended 2nd line regimen:
Abacavir/Zidovudine + Lamivudine + Efavirenz or Nevirapine	<20kg: Abacavir/ Zidovudine + Lamivudine + Lopinavir/ritonavir ≥20kg : 2 NRTIs + Dolutegravir. Ensure at least 1 active NRTI in consultation with an expert
Adverse effects related to Lopinavir/ritonavir Hyperlipidaemia Severe gastrointestinal side effects > 6 weeks Simplification to a once daily regimen	From 6 years and ≥ 15kg: Switch Lopinavir/ ritonavir to Atazanavir/ ritonavir
Failed Protease Inhibitor (PI) or Integrase Strand Inhibitor (InSTI) based regimen	
Abacavir/ Zidovudine/ Tenofovir + Lamivudine/ FTC + Lopinavir / ritonavir or Atazanavir/ritonavir	Diagnose treatment failure if on a PI or DTG based regimen for at least 2 years with virological non-suppression defined as at least three viral load measurements of ≥1000 copies/mL(≥log 3) OR VL>1000 with evidence of clinical or immunological failure. Do genotypic resistance test. If virological non-suppression present but on treatment <2 years, consider doing genotypic resistance test if there is a history of intolerance or poor adherence, non-boosting of a PI-based regimen or no dose adjustment of dolutegravir to overcome a drug interaction. Refer results to the 3rd line ART committee. Should be managed by a Paediatric Infectious Disease Specialist on the basis of genotype resistance testing
Unboosted PI-based regimen	
Abacavir/ Zidovudine/ Tenofovir + Lamivudine/ FTC + Dolutegravir	

*Refer to Annexure 5&6 for standard drug dosages. Refer to Annexure 11 for reporting of adverse drug reactions

5.4 Transition from Paediatric ART regimens to Adolescent/ Adult ART regimens

Adolescents with a suppressed viral load (<50 copies/mL) on ABC+3TC+EFV or ABC+3TC+LPV/r or ABC+3TC+DTG, can transition to TDF+ 3TC +DTG (provide as fixed dose combination) if weight ≥35 kg and older than 10 years.

When an adolescent reach ≥10 years old with weight ≥ 35 kg AND has recent (within last 6 months) suppressed viral load (<50 copies/mL):

- A creatinine clearance (CrCl) and urine dipstix should be performed
- The Counahan Barratt formula should be used to calculate eGFR if <16 years old

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

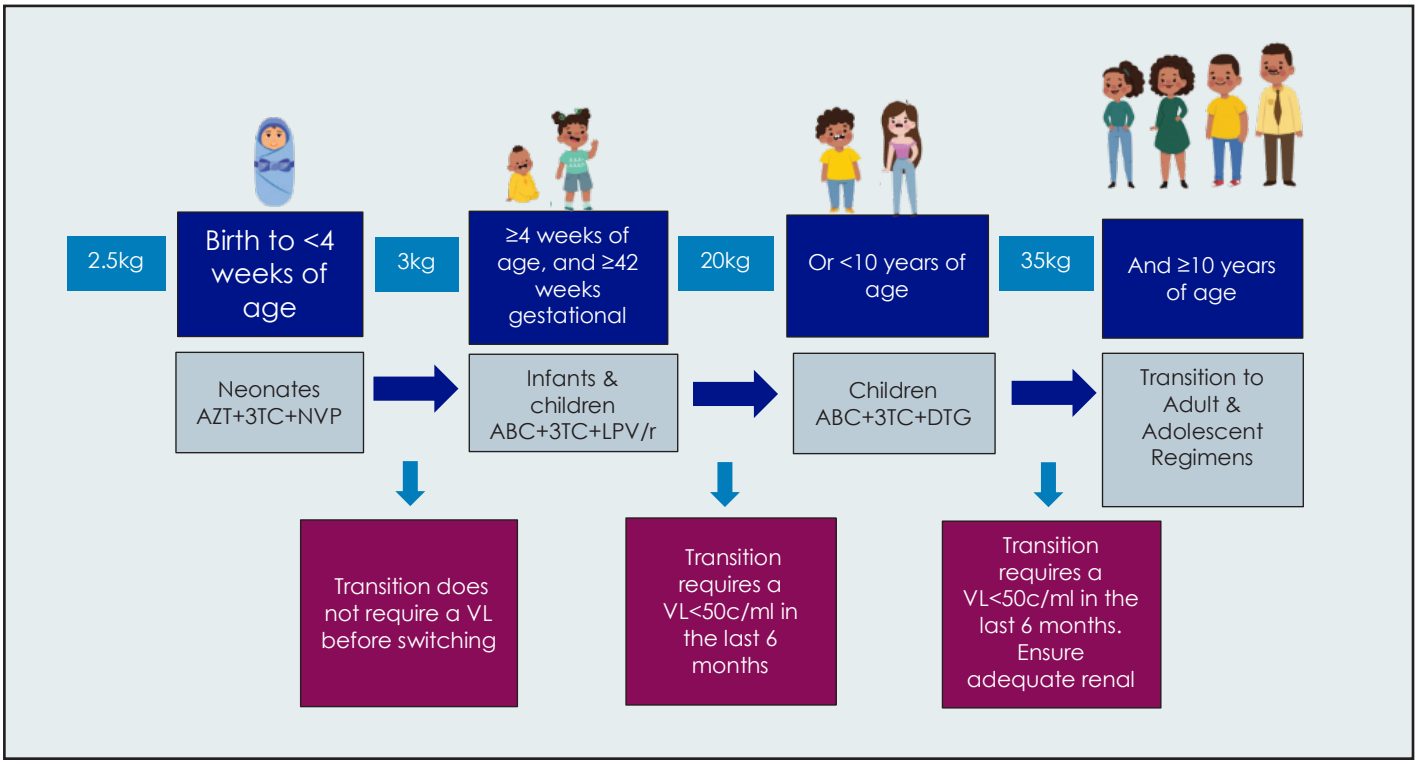
- If the eGFR is >80 mL/min/1.73m² and no proteinuria on urine dipstix, switch to TDF + 3TC + DTG
- If the eGFR is <80 mL/min/1.73m or >1+ Proteinuria on urine dipstix refer to an expert for advice before switching.

If the VL is between 50-999 copies/mL, give adherence support and repeat after 3 months.
If still 50-999, consult an expert for advice.

If the VL is >1000 copies/mL, give adherence support and repeat VL after 3 months.
If still >1000 copies/mL, treat as virological failure

Patients with elevated viral loads must have a thorough assessment of the cause of the elevated VL. See annexure 10.

Figure 6: Summary of ART transitions from Paediatric to Adolescent/ Adult regimens



6. ART IN ADOLESCENTS (10-19 YEARS OLD) & ADULTS

6.1 Eligibility Criteria and Timing of Initiation of ART

Box 6: Eligibility criteria for ART and fast-tracking in late adolescents & adults

Eligibility for starting ART
• All newly diagnosed HIV- positive adolescents and adults are eligible to start lifelong ART regardless of CD4 • Initiate ART within 7 days of diagnosis or on the same day if there are no medical reasons to defer (see table 1) and if patient is ready, as early starting of ART is associated with better health outcomes • Prioritise those with CD4 <350 cells/uL or advanced HIV disease • If the patient refuses to start ART, emphasise benefits of ART and review in 1 month (see box 5)

Patients requiring prioritization	
HIV positive women who are pregnant/breastfeeding Patients with a CD4 ≤ 200 cells/uL Patients with WHO stage 4 disease	Initiate SAME day as eligibility established (if active TB infection and Cryptococcal meningitis excluded)
Patients with TB/HIV co-morbidity with CD4 < 50 cells/uL Patients with DR-TB	Within 2 weeks of commencement of TB treatment

Table 12: Medical Indications to Defer Initiation of ART

Medical Indications to Defer ART	
Indications	**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 TPT after excluding contraindications to TPT (see section 8). If TB is diagnosed, initiate TB treatment and defer ART. The timing of ART initiation will be determined by the site of TB infection and the client's CD4 cell count.
Diagnosis of Drug Sensitive (DS) TB at a non-neurological site (eg. pulmonary TB, abdominal TB, TB lymphadenitis)	Defer ART initiation as follows: • If CD4<50 cells/uL, 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/uL, initiate ART 8 weeks after starting TB treatment
Drug Resistant (DR) TB at a non-neurological site (eg. pulmonary TB, abdominal TB, 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 (eg. TB meningitis, tuberculoma)	Defer ART until 4-8 weeks after start of TB treatment.
Signs & symptoms of meningitis	Refer for investigations for meningitis before initiating ART
Cryptococcal antigen (CrAg) positive in the absence of symptoms or signs of meningitis	Defer ART until 2 weeks of fluconazole prophylaxis has been completed.
Confirmed cryptococcal meningitis	Defer ART until 4-6 weeks after start of antifungal treatment.
Other acute illnesses eg. *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 – check ALT and total bilirubin. ALT elevated >120IU/l with symptoms of hepatitis, and/or total serum bilirubin concentration >40umol/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 any of the above conditions	

Box 7: Management of patients not yet willing to start ART

- Counsel patient on the benefits of ART
- Provide support for disclosure and partner notification. Discuss option of couples counselling and HTS for partner
- Perform TB screening and enquire about TB contacts.
- Initiate TPT if eligible.
- Initiate CPT if eligible
- Screen for and manage sexually transmitted infections (STI's).
- Do Pap smear for women at diagnosis, and repeat every 3 years if no abnormalities detected.
- Advise how to avoid HIV transmission to sexual partners and children.
- Screen for and manage non-communicable diseases
- Provide information and counselling related to fertility, including family planning and conception counselling as needed.
- Provide counselling on nutrition and healthy lifestyle
- Review patient after 1 month or as soon as ready to initiate ART

6.2 Initiation of ART in HIV Positive Partners in Serodiscordant Couples

Box 8: Approach to ART in serodiscordant couples

Importance of ART in Serodiscordant Couples

- A couple is defined as two people involved in an ongoing sexual relationship.
- A serodiscordant couple is one in which one partner is HIV-positive and the other is HIV- negative.
- Research shows that about half of all people infected with HIV are in serodiscordant couples.
- HIV transmission to HIV-negative partners in serodiscordant couples can effectively be prevented by the use of ART by their HIV-positive partners.

General Approach to ART in Serodiscordant Couples

- All patients presenting for HTS should be offered the option of couples HTS.
- Pregnant women must be tested on the day pregnancy is confirmed; therefore, do not postpone testing until the partner is available. If the partner is present, offer same-day couples counselling and HTS. If unavailable, make effort to test the partner as soon as possible and offer the option of couples HTS for repeat tests. If the patient tests HIV-positive at any stage, she is immediately eligible for ART (see PMTCT section). Partners who test HIV-positive should also be initiated on ART.
- All patients who test HIV-positive after HTS should receive post-test counselling with support for disclosure to their partners.
- Pre-ART counselling should include information about the benefits and risks of ART. Couples should be advised to continue using condoms, and to repeat HTS for the HIV-negative partner every 6 months.
- Patients on ART and their partners should be encouraged to access available health services for TB screening, NCD screening, treatment of STI's, family planning and conception counselling.

6.3 Monitoring of Adolescents & Adults on ART

Table 13: Monitoring in late adolescents & adults on ART

At initial Diagnosis of HIV	Purpose
Confirm HIV status	To confirm HIV positive status in clients who present without documented proof of positive HIV status. Ensure that Western Cape testing algorithm has been followed
Baseline CD4 count and WHO clinical staging	To assess eligibility for: prioritization (CD4 ≤350) Cotrimoxazole prophylactic treatment (CPT) (CD4 < 200 cells/µl) (section 9) Eligibility for reflex CrAg (CD4 < 100) (section 10) For all newly diagnosed or known HIV positive pregnant women at first antenatal booking- to assess eligibility for TPT
Screen for pregnancy or ask if planning to conceive	To identify pregnant women eligible for ART, opportunity to offer appropriate family planning/ conception counselling
For women, do Pap smear if not done in previous 3 years	To screen for cancer of the cervix. Repeat pap smear routinely every 3 years
Screen for TB symptoms and close TB contacts	To identify TB/HIV co-infection (refer to TB screening tool (annexure 10) If CD4<100 cells/µl, clinical stage 4 or ill, screen for TB using TB GeneXpert and urine LF-LAM
Sputum for TB GeneXpert test for all symptomatic patients, all pregnant known HIV positive women at first antenatal booking and all women newly diagnosed HIV positive during pregnancy regardless of symptoms	To diagnose TB in HIV positive patient, (sensitivity of the TB symptom screen is lower in pregnant women)
Screen for STI's and syphilis (do RPR)	To manage STI's and provide counselling on prevention of STI's and condom use
Screen for major non- communicable diseases (diabetes, hypertension)	To identify any concomitant chronic disease. Check blood pressure and check for protein and glucose on urine dipstix
Screen for symptoms of common mental illnesses (depression, anxiety, substance abuse)	To identify and manage mental illnesses that can impact on adherence to ART and other chronic medications. Use available symptom screening tool.
Weight and Height in adolescents	To determine appropriate ART regimen
Cryptococcal antigen (CrAg) : If baseline CD4<100 cells/mm³ (reflex test done routinely by lab if CD4<100)	To identify patients who require treatment or prophylaxis for Cryptococcal Meningitis (CM) (refer to section 10)
FBC + differential WCC: for clients initiating on AZT	To detect anaemia/neutropaenia
ALT: for clients initiating on NVP	To detect liver dysfunction
Serum creatinine for clients initiating on TDF (The NHLS uses the MDRD formula to calculate creatinine clearance for patients > 18 years and reports eGFR. This is an acceptable approximation of creatinine clearance and can also be used) In adolescents <16 years: DO NOT use TDF if CrCl ≤80. In adults/ adolescents ≥16 years: DO NOT use TDF if CrCl ≤ 50. In pregnant women : DO NOT use TDF if serum creatinine ≥ 85 µmol/l Refer to section 6.4 for alternate regimens. Doses of ARV's may need to be adjusted for renal impairment. Refer to annexure 8.	To detect renal insufficiency- calculate creatinine clearance (CrCl) as shown below: If < 16 years: use Counahan Barratt formula: eGFR [mL/min/1.73m²] = height [cm] x 40 / serum creatinine [µmol/L] If ≥ 16 years, use adult formula (modified Cockroft and Gault formula): eGFR [mL/min] = (140 – age) x Wt (kg) / serum creatinine (µmol /L) Females: multiply CrCl by 0.85 If the CrCl is abnormal (<50mL/min for adults or <80mL/min for children): Check urine dipstix for proteinuria and repeat serum creatinine after 1 month. Do not initiate TDF. Refer to experienced clinician if renal dysfunction persistent

On ART	Purpose
CD4: All at **month 12** Then: Repeat CD4 **every 6 months until meet criteria to discontinue CPT** If at any later stage VL ≥1000 c/mL on 2 consecutive tests, repeat CD4 every 6 months to monitor for immunological failure Restart CPT if indicated.	To monitor susceptibility to opportunistic infections. Stop prophylactic cotrimoxazole if CD4>200 cells/mm³ and no concurrent stage 3/4 infection present.
VL on 1st line regimen: at month **4, month 12 and then annually** VL on 2nd and 3rd line regimens: at month 6, month 12 and then annually If on DR-TB treatment: repeat VL every 6 months until DR-TB treatment completed. **If VL 50-999c/mL**, repeat after 3 months. If unchanged, consult a specialist for advice. **If VL >1000**, repeat within 3 months (2 months after adherence intervention). If second VL >1000 c/mL, manage as virological failure (refer to section 6.5) If pregnant or breastfeeding, refer to section 2 for VL monitoring	To monitor response to treatment and detect treatment failure Patients with elevated viral loads must have a thorough assessment of the cause of the elevated VL. See annexure 10. Provide intensive adherence counselling, review drug tolerability/ side-effects/ drug interactions and assess any psychological issues.
Serum creatinine: **at month 1, 4, 12** and then annually if on TDF	To detect TDF toxicity- calculate CrCl (see formulae above) or use laboratory reported eGFR
ALT: If on NVP or EFV and develops rash or symptoms suggestive of hepatitis If on TB treatment and Lopinavir/ritonavir	To detect clinical signs of NVP or EFV toxicity At weekly intervals, check ALT and increase LPV/r to 3 and then 4 tablets every 12 hours if ALT <50 If ALT <50 on 4 tablets every12 hours: check ALT monthly for duration of TB treatment If ALT 50 -199 and client well: continue treatment and repeat in a week. If ALT >200 or unwell: stop ART and refer on the same day. Reduce LPV/r to standard dose 2 weeks after TB treatment is completed.
FBC and differential WCC: **at month 1, 3 and 6** if on Zidovudine	To detect AZT toxicity
Total cholesterol and triglycerides (random or fasting) Repeat annually only if clinically indicated.	To detect lopinavir /ritonavir toxicity If total cholesterol >6mmol/l/ or triglycerides >5mmol/l, consider switch to Atazanavir/r. Management of hyperlipidaemia may include dietary modification and statins as per EML/STG. Refer if triglycerides>10mmol/l.
HBsAg	To identify hepatitis B co-infection in patients on TDF switching to 2nd line regimens so that TDF can be retained in the second line regimen.
Routine Pap smear for all women on ART every 3 years if no abnormalities detected. If abnormalities detected, repeat after 6 months or refer for colposcopy (as advised by the laboratory report).	To detect pre-cancerous/ cancerous lesions of the cervix

6.4 Standard 1st Line Drug Regimens for ART in Adolescents & Adults

Table 14: Standard 1st line ART regimens for adolescents & adults

1st Line Regimens*		
Indications	**Regimen**	**Comments**
Initiation of ART in adolescents & adults eligible for DTG (see section 2.2)	Tenofovir + Lamivudine + Dolutegravir Provide as fixed dose Combination	Use TDF in adolescents only if ≥10 years old AND ≥35kg AND eGFR≥ 80 mL/min/1.73m² (see section 6.3 for formula to calculate eGFR) Use TDF in adults only if eGFR > 50mL/ min/1.73m² or serum creatinine <85 µmol/l in pregnant women
Initiation of ART in patients not eligible for DTG-containing regimens (see section 2.2)	Tenofovir + Emtricitabine + Efavirenz Provide as fixed dose Combination	
Contraindications to Tenofovir	Abacavir + Lamivudine + Dolutegravir	Renal disease: (eGFR ≤ 50 mL/mL in adults; eGFR <80 mL/min/1.73m² in adolescents; eGFR < 85 mL/min in Pregnant women)
Contraindications to Tenofovir and Abacavir	Zidovudine + Lamivudine + Dolutegravir	Hypersensitivity to Abacavir Renal disease: (eGFRl ≤ 50 mL/mL in adults; eGFR <80 mL/min/1.73m² in adolescents; eGFR < 85 mL/min in pregnant women)
Patients on NNRTI based regimens might be eligible to switch to a dolutegravir based regimen. Refer to section 2.		

*Refer to Annexure 7 & 8 for standard drug dosages, side-effect profiles and drug- dosing in renal dysfunction. Refer to Annexure 14 for reporting of adverse drug reactions.

6.5 Standard 2nd Line drug regimens for ART in Adolescents & Adults

- Virological failure in a patient on a 1st line dolutegravir containing regimen is diagnosed when VL>1000 c/mL on at least three occasions over the course of two years. This is an indication to switch to a 2nd line regimen.
- Virological failure in a patient on a 1st line NNRTI based regimen is diagnosed when VL > 1000 c/mL on two separate occasions 2-3 months apart.
- If a patient is on a Tenofovir -based regimen, check Hepatitis B status (HBsAg) before switching regimens to establish if Tenofovir must be retained.
- If a patient is pregnant or breastfeeding, switch regimens on same day, but retain Tenofovir in the new regimen until Hepatitis B status is known.
- The choice of ARVs in the 2nd line regimen will depend on the composition of the 1st line regimen- refer to table 15.

Table 15: Standard 2nd line ART regimens for adolescents & adults

2nd Line Regimens*		
Indications	**Regimen**	**Comments**
Failing on Tenofovir + Emtracitabine + Efavirenz / Nevirapine with HBsAg positive	Tenofovir + Zidovudine + Lamivudine/ Emtricitabine + Dolutegravir	If dolutegravir not suitable, tenofovir + lamivudine/ emtricitabine + Lopinavir/r
Failing on Tenofovir + Emtracitabine + Efavirenz/ Nevirapine with HBsAg negative	Zidovudine + Lamivudine + Dolutegravir	If HB <8, consult an expert If dolutegravir not suitable, zidovudine + lamivudine + Lopinavir/r
Failing on Abacavir+ Lamivudine+ Efavirenz/ Nevirapine	Zidovudine + Lamivudine + Dolutegravir	
Failing on Abacavir+ Lamivudine+Efavirenz Zidovudine and tenofovir are contraindicated	Consult an expert	Hb ≤ 8 g/dl + renal impairment.
Failing on Zidovudine+ Lamivudine+ Efavirenz Tenofovir contraindicated	Consult an expert	Renal impairment
Adverse effects related to Lopinavir/ritonavir • Hyperlipidaemia: Total Cholesterol >6mmol/l fasting triglycerides > 5mmol/l • Cardiovascular event risk > 20% • Established clinical cardiovascular disease • Severe gastrointestinal side effects > 6 weeks	Switch Lopinavir/ ritonavir to Atazanavir/ ritonavir	Advise dietary modifications and refer to medical officer.
Failing Tenofovir + Lamivudine + Dolutegravir for > 2 yrs with HBsAg positive	Tenofovir + emtricitabine + Lopinavir/r	
Failing Tenofovir + Lamivudine + Dolutegravir for > 2 yrs with HBsAg negative	Zidovudine + lamivudine + Lopinavir/r	If HB <8, consult an expert

*Refer to Annexure 7&8 for standard drug dosages, side-effect profiles and drug- dosing in renal dysfunction. Refer to Annexure 11 for reporting of adverse drug reactions.

6.6 Third Line Drug Regimens for ART in Adolescents & Adults

If a patient has virological failure on a 2nd line regimen containing a PI or InSTi, a decision to switch to a new regimen will be based on the results of genotype resistance testing (*Provincial circular H158/2014*). Access to 3rd line ART will be managed centrally by the HAST Directorate at the Provincial Department of Health (refer to annexure 8 for application forms). There is no empiric 3rd line regimen and consideration of an appropriate regimen will be individualised according to the results of the genotypic resistance test and a complete drug history.

Resistance tests are costly and studies show that most patients failing ritonavir-boosted Protease Inhibitors (PIs) or DTG- based regimens do not have resistance mutations. Resistance testing will only be offered to patients with good adherence, assessed objectively by means of pharmacy dispensing refills and the completed adherence evaluation form, submitted along with the application.

Indications for resistance testing in adults and adolescents:

- Patients on a PI or InSTi based regimen for >2 years with virological non-suppression defined as at least three viral load measurements of ≥1000 copies/mL OR viral load >1000 with evidence of clinical and/or immunological failure
- Patients on a PI or InSTi based regimen for <2 years with virological non-suppression and a history of non-boosting of a PI-based regimen or no dose adjustment of dolutegravir to overcome a drug interaction.

ARV's in 3rd line regimens may include boosted Darunavir, Dolutegravir or Etravirine according to genotype interpretation and patient history.

6.7 Indications for Referral to a Medical Officer

- Baseline creatinine clearance less than 50 mL/min
- Increase in serum creatinine after initiation of Tenofovir
- Decrease in Hb after initiation of Zidovudine
- Poor response to TB treatment or suspicion of TB IRIS
- Change in clinical stage of disease while on ART
- Any clinical suspicion of drug-induced liver injury (DILI) relating to efavirenz, TB drugs or any of the other ART drugs (persistent nausea, abdominal discomfort or jaundice)
- Clinical signs of possible meningitis: e.g. confusion; headaches
- Psychiatric illness

6.8 Family Planning and Reproductive Choices for Patients on ART

Discuss family planning and conceptive options with all clients on ART. Advocate for the use of dual protection if no pregnancy is planned. Due to concerns around the safety of DTG in the periconception period, 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.

For women planning a pregnancy:

- Enquire about the HIV status of the partner - if unknown, advise HTS and offer couple's counselling. If partner is HIV-positive, refer him to clinician to optimise HIV management.
- Check patient's general health, review WHO stage and latest blood test results.
- Screen for TB and STIs.
- Review latest Pap smear result or refer for Pap smear if not done in preceding three years.
- Optimise HIV management, refer to medical officer if most recent viral load >1000 or any other medical problems present.

6.9 Strategies to Promote Adherence in Late Adolescents & Adults on ART

- Pre-ART adherence counselling should be offered to all clients.
- Disclosure to supportive family or friends should be encouraged.
- Discuss minor/transient side effects with the client.
- Monitor adherence and offer adherence support at every visit.
- Aim for adherence of >95% of doses taken.
- Patients with elevated viral loads must have a thorough assessment of the cause of the elevated VL. See annexure 10.
- Patients who miss appointments are more likely to have poor adherence, and therefore require additional adherence support.
- Manage prolonged side effects or adverse effects appropriately.
- Identify threats to adherence such as substance abuse, food insecurity and gender-based violence and refer appropriately.
- Patients with issues about stigma, non-disclosure and poor adherence should be referred for on-going counselling.
- Patients should be informed about ART Adherence Clubs, and should be enrolled in these clubs as soon as they are eligible, if feasible.

6.10 Management of patients transferring into a facility from another facility

- Establish the clinical history from the patient and review any documents available.
- Try to establish which regimen the patient is currently on and the treatment duration. Review any previous CD4/VL /other blood test results.
- If unable to access blood results, do CD4, VL and monitoring bloods. Screen for TB, STI and NCDs.
- Continue previous/ most appropriate regimen.
- Give patient appointment to follow up for blood results.

6.11 Management of patients returning to care after period of treatment interruption

A growing number of PLHIV are returning to care after a period of disengagement presenting with advanced HIV disease and are at a high risk of death from serious opportunistic infections such as TB, severe bacterial infections and cryptococcal meningitis (less common among children), even after starting ART. The WHO recommends a defined package of care interventions, which includes screening, treatment and prophylaxis for major opportunistic infections, rapid initiation of ART and intensified treatment adherence support for people representing to care with advanced HIV disease to reduce HIV associated morbidity and mortality.

Identify the client returning to care who needs urgent attention & referral:

- Breathlessness at rest or while talking
- Respiratory rate ≥ 30 breaths/minute, heart rate >120 beats per minute, BP < 90 (systolic)
- Prominent use of breathing muscles
- Coughing up ≥ 1 tablespoon of fresh blood
- Unable to stand/walk unaided
- Confusion or agitation
- Symptoms of meningitis: headache, neck stiffness, fever

If none of above signs present and client is stable, assess and manage according to table 16.
If no sign of TB or meningitis, restart ART on same day.
Choice of ART regimen:

- If a patient has interrupted treatment on a known regimen, and is currently well with no clinical suspicion of TB, he/she should be restarted on the same day with the same regimen. If previous regimen unknown, consult an expert.
- If patient was on a 1st line regimen before treatment interruption, consider starting a 2nd line regimen If there is a history of multiple treatment interruptions and resistance to the regimen is considered likely, or the patient is now very ill with an AIDS-defining condition and a CD4 count < 50 cells/mL as this carries a high risk of mortality. Consult a medical officer if unsure of which regimen to restart.

Viral Load Monitoring:

- Check VL 3 months later.
- If VL<50 c/mL, continue current ART regimen.
- If VL between 50-999 c/mL. Provide intensive adherence counseling, review drug tolerability/ side effects/ drug interactions and assess any psycho-social issues. Repeat VL after 3 months. If still in same range, consult an expert.
- If VL ≥1000 c/mL. Provide intensive adherence counseling, review drug tolerability/ side effects/ drug interactions and assess any psycho-social issues. Repeat VL after 3 months. If still ≥1000 c/mL, manage as treatment failure.
- If patient is pregnant or breastfeeding- refer to section 3.
- Provide adherence counselling & support at every visit
- Patients with elevated viral loads must have a thorough assessment of the cause of the elevated VL. See annexure 10.

Table 16: Management of Stable Client Returning to Care after period of Treatment Interruption

Baseline Assessment	
Treatment History	Previous ART regimen & duration of treatment Reasons for stopping ART Previous VLs done whilst on ART Previous CD4 count Co-morbid conditions (eg diabetes, hypertension, mental illness, substance abuse)
Screening: TB, Opportunistic infections, STIs, NCDs, Pregnancy	Clinical signs & symptoms of TB Close TB contacts Severe headache, fever, chronic diarrhea Symptoms of STI Blood pressure & urine dipstix- glucose & protein Pregnancy test if indicated
TPT eligibility (see section 8)	History of TB treatment History of previous TPT Contraindications to TPT
Baseline Investigations	
Baseline bloods	CD4 count Creatinine FBC & diff RPR
Sputum TB GeneXpert	If any symptoms of TB present
Urine LF-LAM	If any symptoms of TB present and CD4<100 cells/ml (see annexure 13)
Treatment Initiation on Same Day	
Cotrimoxazole Prophylaxis (CPT)	Start CPT regardless of previous CD4 count
ART	Restart ART if no symptoms of TB or meningitis
TPT	Start TPT if eligible & no symptoms of TB
Medical reasons to Defer Initiation of ART	
Refer to table 12	
Follow-up within 1 week	
TB GeneXpert result (refer to annexure 11)	If positive, start TB treatment. If negative and client symptomatic, refer to medical officer for assessment
Blood results	If CD4<100 cells/uL, review reflex CrAg result. If positive and symptomatic refer for LP. If positive and asymptomatic start fluconazole pre-emptive therapy (section 10), and delay ART initiation for 2 weeks if not already started. If ART already started, continue ART. If CrAg negative, continue ART. If eGFR<50mmol/mL or Hb <8g/dL, discuss with an experienced MOIf Hb<8g/dL switch AZT to ABC Review need for CPT.

7. MANAGEMENT OF PATIENTS CO-INFECTED WITH TUBERCULOSIS (TB)

HIV-infected people have an increased risk of developing TB disease compared to people not infected with HIV. They should be screened for TB symptoms at every clinic visit. Patients co-infected with TB are eligible for lifelong ART regardless of CD4 count.

Suspect TB if any of the following symptoms are present:

- Cough of any duration
- Blood-stained sputum
- Fever
- Drenching night sweats
- Unexplained weight loss
- Loss of appetite, malaise, tiredness
- Chest pain on breathing

In children - suspect TB if the following are present:

- Any symptoms of TB as listed above
- Failure to thrive
- Clinical signs suggestive of TB
- Positive TST
- Chest X-ray findings suggestive of TB

7.1.1 Management of the patient that presents with TB before commencing ART

- All patients who are HIV positive and on TB treatment are eligible for ART regardless of CD4 count. (Refer to table 12 for timing of ART initiation)
- The importance of keeping patients in care should be considered and patients should be offered adherence support at every visit.

Table 17: Timing of ART initiation in HIV co-infected patients

TB diagnosed before starting ART	
Diagnosis of DS-TB at a non-neurological site (eg. Pulmonary TB, abdominal TB, or TB lymphadenitis)with a CD4 count <50 cells/uL or CD4<15% in children	Initiate on ART within 2 weeks of starting treatment, when TB symptoms are improving and TB treatment is tolerated
Diagnosis of DS-TB at a non-neurological site with CD4 >50 copies/uL or >15% in children	Start ART 8 weeks after starting TB treatment in adolescents & non-pregnant adults. In children, start ART after 2-8 weeks of TB treatment, when TB symptoms are improving and TB treatment is tolerated.
Diagnosis of DR-TB at a non-neurological site	Initiate ART after 2 weeks of TB treatment, when TB symptoms are improving and TB treatment is tolerated
Diagnosis of DS-TB or DR-TB at neurological site (eg. TB meningitis or tuberculoma)	Defer ART 4 – 8 weeks after start of TB treatment

Table 18: Management of patient who develops TB and not on ART

Recommended ART regimen if patient develops TB while not on ART		
	DS-TB (rifampicin-containing regimen)	DR-TB
Children <10 years old		
Never received ART before,	Children <20kg, Abacavir + Lamivudine + Lopinavir/Ritonavir Requires super-boosting of LPV/r- see annexure 5 Children/ adolescents 20-35kg Abacavir + Lamivudine + Efavirenz	Children <20kg, Abacavir + Lamivudine + Lopinavir/ Ritonavir Children/ adolescents 20-35kg Abacavir + Lamivudine + Dolutegravir
Previously on ART but not currently on ART	Discuss with expert	Discuss with expert
Adolescents ≥10 years old and > 35kg & Adults		
Never received ART before	Initiate Tenofovir + Emtracitabine + Efavirenz If TDF contraindicated, initiate: Abacavir + Lamivudine + Efavirenz If pregnant, initiate Tenofovir + Lamivudine + Dolutegravir. Give second dose of Dolutegravir 50mg 12 hours after daily dose of TLD until 2 weeks after completion of TB treatment.	Initiate Tenofovir + Lamivudine + Dolutegravir If TDF contraindicated, initiate: Abacavir + Lamivudine + Dolutegravir
Not currently on ART but previous ART regimen: Tenofovir + Emtracitabine + Efavirenz OR Abacavir + Lamivudine + Efavirenz	Restart the same regimen unless CD4<50 copies/ uL or patient is very ill- consider starting a 2nd line regimen. Do VL in 3 months. If pregnant, start DTG-containing 1st or 2nd line regimen (see table 3)	Start Tenofovir+ Emtracitabine + Lopinavir/ritonavir OR Abacavir+Lamivudine+ Lopinavir/ ritonavir. Do VL in 3 months
Not currently on ART but previous ART regimen: Zidovudine/ Abacavir + Lamivudine + Lopinavir/ ritonavir	Restart the same regimen. Check ALT at baseline and adjust doses of Lopinavir/ritonavir as follows: (Double dosing schedule only if able to swallow LPV/r tablets. See annexure 5 for super-boosting in children with other LPV/r formulations) If ALT <50, increase from 2 tablets every 12 hours to 3 tablets every 12 hours. Check ALT after 1 week. If ALT <50, increase from 3 tablets every 12 hours to 4 tablets every 12 hours. Check ALT after 1 week. If ALT <50 on 4 tablets every 12 hours: check ALT monthly for duration of TB treatment If ALT 50 -199 and no symptoms of hepatitis continue treatment and repeat in a week. If ALT >200 or symptoms of hepatitis: stop ART and refer on the same day. Reduce Lopinavir/ritonavir to standard dose 2 weeks after TB treatment is completed.	Restart Abacavir + Lamivudine + Lopinavir/ritonavir. Do VL in 3 months

7.1.2 Prevention of Paradoxical TB Immune Reconstitution Inflammatory Syndrome (TB-IRIS)

TB Immune Reconstitution Inflammatory Syndrome (TB-IRIS) occurs in 8-54% of patients initiating ART while on treatment for TB. Patients present within 1-3 weeks of starting ART with recurrent or worsening symptoms and inflammatory features of TB, after showing signs of improvement prior to starting ART. TB-IRIS symptoms may last for 2-3 months.

The earlier a patient starts ART, the higher the risk of developing TB-IRIS. But concern about TB-IRIS is NOT a reason to delay ART in patients with low CD4 counts; early ART in such patients reduces mortality. Patients with CD4 count<100 are at higher risk of developing TB-IRIS compared to patients with a higher CD4 count.

A recent study found that prophylactic prednisone may reduce the incidence of TB-IRIS in certain patients. In the study the incidence of TB-IRIS was 30% lower in participants who received prednisone compared to those who received placebo (i.e. prednisone reduced the risk but did not prevent all cases).

Guideline for use of prophylactic prednisone to prevent TB- IRIS:

Eligible patients:

- HIV-infected 18 years or older, **and**
- Diagnosed with TB within the last month, **and**
- Symptoms improving on TB treatment, **and**
- CD4 ≤ 100, **and**
- Not yet on ART

Exclusions:

- Rifampicin resistant TB
- Kaposi's Sarcoma
- Poor clinical response to TB treatment

Dosage & duration of prophylactic prednisone:

- Start prednisone on the same day as ART
- 40mg daily orally for 2 weeks, followed by
- 20mg daily orally for 2 weeks then stop

Any patient who experiences deterioration in their clinical condition after initiation of ART should be referred to an experienced clinician immediately for further management. The deterioration could be due to TB-IRIS, drug side effect, drug-resistant TB or another infection, and such patients need urgent assessment.

7.2 Management of the patient that presents with TB while on ART

Table 19: Management of Patients who Develop TB while on ART

Recommended ART regimen if patient develops TB while on ART		
Current ART Regimen	**DS-TB (rifampicin-containing regimen)**	**DR-TB**
Children <10 years old		
Abacavir + Lamivudine + Lopinavir/Ritonavir	Continue same regimen Requires super-boosting of LPV/r- see annexure 5	Continue same regimen
Abacavir + Lamivudine + Efavirenz	Continue same regimen	Discuss with expert
Abacavir + Lamivudine + Dolutegravir	Continue same regimen Add 50mg dose of Dolutegravir 12 hours after usual daily dose of ART Discontinue additional dose of Dolutegravir 2 weeks after stopping TB treatment	Continue same regimen
Adolescents ≥10 years old & Adults		
Tenofovir /Abacavir + Lamivudine/Emtricitabine + Efavirenz	Continue same regimen	If VL<50 c/mL, switch efavirenz to dolutegavir and retain the NRTI backbone If VL≥50 c/mL switch tefavirenz ot Lopinavir/r and retain NRTI backbone
Tenofovir/Abacavir + Emtricitabine + Dolutegravir	Continue same regimen Add 50mg dose of Dolutegravir 12 hours after usual daily dose of combination ART Discontinue additional dose of Dolutegravir 2 weeks after stopping TB treatment	Continue same regimen
Zidovudine + Lamivudine + Dolutegravir		Discuss with expert
Zidovudine/ Abacavir + Lamivudine + Lopinavir/ ritonavir	Continue same regimen. Check ALT at baseline and adjust doses of Lopinavir/ritonavir as follows: (Double dosing schedule only if able to swallow LPV/r tablets. See annexure 5 for super-boosting in children with other LPV/r formulations) If ALT <50, increase from 2 tablets every 12 hours to 3 tablets every 12 hours. Check ALT after 1 week. If ALT <50, increase from 3 tablets every 12 hours to 4 tablets every 12 hours. Check ALT after 1 week. If ALT <50 on 4 tablets every 12 hours: check ALT monthly for duration of TB treatment If ALT 50 -199 and client well: continue treatment and repeat in a week. If ALT >200 or unwell: stop ART and refer on the same day. Reduce Lopinavir/ritonavir to standard dose 2 weeks after TB treatment is completed.	Abacavir + Lamivudine + Lopinavir/ ritonavir

7.3 Drug Interactions with ART and TB Treatment

Rifampicin

- There are significant drug interactions between Rifampicin and certain ARVs, therefore substitute Rifampicin with Rifabutin in the following patients:
  - Adult patients on **Lopinavir boosted with ritonavir,** who are initiated on concomitant Rifampicin-based TB treatment and are unable to tolerate double dose LPV/r due to severe GIT side effects or hepatitis.
  - Adult patients on Atazanavir boosted with ritonavir, who require initiation of rifampicin-containing TB treatment.
  - Adult patients on Darunavir boosted with ritonavir, who require initiation of Rifampicin-containing TB treatment.
- Doses may need to be adjusted-refer to table 20.
- Rifabutin's main active metabolite is increased about tenfold when given with protease inhibitors compared with the usual dose of 300 mg daily. The 150-mg daily rifabutin dose with protease inhibitors might increase the risk of toxicity (especially uveitis, neutropenia, and hepatitis), which is related to concentrations and thought to be due in part to the rifabutin metabolite.
- Patients on Darunavir boosted with ritonavir in combination with Etravirine requiring Rifamycin-containing TB treatment should not be started on Rifampicin or Rifabutin. Refer to an HIV specialist for guidance on anti-TB and ART regimen.
- Dosage of Dolutegravir must be doubled whilst patients are on rifampicin

Table 20: Dose adjustments of Rifabutin for patients on ART

Dose Adjustments of Rifabutin for Patients on ART	
Rifabutin standard dose	300 - 450mg capsule orally once daily for 6 months of TB treatment
Rifabutin adjusted dose when prescribed with Ritonavir boosted protease inhibitors (Lopinavir or Atazanavir or Darunavir)	150mg capsule orally once a day for 6 months of TB treatment

Bedaquiline

- Avoid concurrent use with efavirenz as it can decrease bedaquiline AUC by 50%
- Replace with dolutegravir if VL <50 c/mL
- Replace with boosted PI if VL ≥50 c/mL
- Avoid concurrent use with etravirine

Linezolid

- Avoid concurrent use of zidovudine
- Additive mitochondrial and haematotoxicity if used with Zidovudine
- Replace with abacavir for duration of treatment with Linezolid
- Monitor FBC/diff monthly

8. TB PREVENTIVE THERAPY (TPT) FOR TB CONTACTS & HIV INFECTED PATIENTS

- All patients in HIV care must be screened for symptoms of active TB at every clinic visit
- TPT is an effective intervention for preventing the development of active TB disease in clients with latent TB infection, and should be given to eligible children and adults
- However, the use of TPT with isoniazid during pregnancy has been associated with a higher risk of adverse infant outcomes, therefore it is now recommended that TPT only be given to eligible clients with CD4<100 cells/µL during pregnancy, and that TPT initiation is delayed to 6 weeks after delivery for clients with CD4≥100 cells/µL

8.1 TPT for Contacts of TB-Infected Clients

Infants, Children & Adolescents <15 years old

- Indications:
    - All asymptomatic children <5 years of age or HIV infected irrespective of age in close contact with an infectious pulmonary TB case and a clinically normal chest X-ray.
    - HIV infected children 5-14 years without history of close contact but TST positive.
    - Newborn infants of mothers with active TB should be managed in line with the National TB guidelines. Infants should be monitored for active TB disease during prophylaxis and if asymptomatic for TB after 6 months, should be given BCG.

- Children who are re-exposed to TB following completion of TPT must repeat the course of therapy.
- This is not dependent on the interval between completion of treatment and re-exposure.
- Pre-exposure TPT is not recommended in HIV infected children.
- Children who have successfully completed TB treatment should not routinely receive TPT. In the event of a new adult infectious TB source case, refer to an expert for advice.
- Refer to an expert if:
    - there was close contact with a known drug resistant TB source case
    - there was close contact with a contact of a known drug resistant TB source case
    - there was close contact with a TB source case who has failed standard TB treatment

- TPT post-exposure to DS-TB (Rifampicin-susceptible):
    - Isoniazid 10mg/kg/day (maximum 300mg daily) (see table 19)with Pyridoxine (<5 years - 12.5 mg daily, ≥5 years - 25 mg daily)

- TPT post-exposure to DR-TB (Rifampicin-resistant):
    - Levofloxacin 15-20 mg/kg/day + high dose Isoniazid 15-20 mg/kg/day (maximum 400mg daily) + Ethambutol 15-25 mg/kg/day with Pyridoxine (<5 years - 12.5 mg daily, ≥5 years - 25 mg daily)

- Duration of TPT: 6 months

<u>Adolescents ≥15 years old & Adults:</u>

- Eligible for TPT if known HIV positive
- Screen for symptoms of TB and test for TB if indicated
- If no TB symptoms, give TPT
- Dose: see section 8.3
- Duration: 1 year unless but if previously completed 1 year course give for 6 months

8.2 TPT for Adolescents≥ 15 years old & Adults with HIV Co-infection

- TPT is an effective intervention for preventing the development of active TB disease in clients with latent TB infection
- All HIV infected adolescents ≥15 years old and adults should be assessed for TPT unless the following
- contraindications are present:
    - Active TB (suspected or confirmed)
    - Known or suspected hypersensitivity to INH
    - Chronic or acute liver disease
    - History of excessive alcohol use >28 units per week in men or >21 units per week in women
    - Severe peripheral neuropathy
    - Patients who have completed MDR- or XDR-TB treatment

- TPT (using isoniazid) during pregnancy is associated with an increased risk of poor outcomes, therefore it should not be initiated during pregnancy unless CD4<100. If CD4≥ 100, defer TPT until after delivery.
- TPT is safe to use during breastfeeding
- Do not give TPT to HIV positive client that has recently completed course of TB treatment

- How to Initiate and Manage TPT:
    - Dosing: Isoniazid 10mg/kg/day (maximum 300mg daily) (see table 19) with Pyridoxine 25mg daily.
    - Duration: HIV positive adolescents ≥15 years and adults should receive and complete TPT for a duration of 12 months
    - Screen clients on TPT for symptoms of active TB and side-effects of treatment at every clinic visit for duration of treatment.

Table 21: Dosing of INH for TPT

INH Dosing Chart		
Oral Isoniazid (INH) 10mg/kg daily for 6 months Maximum dose 300 mg daily		
Weight	**Daily dose**	**Daily number of tablets (100mg)**
2-3.4 kg	25mg	¼ tablet
3.5-6.9 kg	50mg	½ tablet
7-9.9 kg	100mg	1 tablet
10-14.9 kg	150mg	1 ½ tablets
15-19.9 kg	200mg	2 tablets
20-24.9 kg	250mg	2 ½ tablets
≥25 kg	300mg	3 tablets

9. COTRIMOXAZOLE PREVENTIVE THERAPY (CPT)

9.1 CPT in Children

- Cotrimoxazole Preventive Therapy (CPT) provides protection against Pneumocystis Jiroveci pneumonia (PCP), toxoplasmosis, malaria and other bacterial infections.

Table 22: Indications for CPT

Age & HIV Status	When to Start	When to Stop
HIV-exposed infants who are HIV negative	Start CPT 4-6 weeks after birth	Continue CPT whilst breastfeeding, stop CPT once HIV infection is excluded with HIV test 6 weeks after final breastfeed AND infant is clinically HIV negative
HIV positive infant <1 year old	Start CPT 4-6 weeks after birth, irrespective of clinical stage or CD4 count	Continue CPT until meets criteria to stop when >1 year old
HIV positive child 1-5 years old	Eligible for CPT if WHO clinical stage 2, 3 or 4; CD4 <25%	Stop CPT if CD4≥25% , regardless of clincical stage
HIV-positive child < 5 years with PJP infection	Start CPT after PJP treatment completed	Continue CPT until 5 years old, then stop CPT if CD4≥200 cells/µl, regardless of clinical stage
HIV-positive child ≥5 years old	Eligible for CPT if WHO clinical stage 2, 3 or 4; CD4 <200 cells/uL	Stop CPT if CD4≥200 cells/ l, regardless of clinical stage
HIV- positive child with TB at any age	Eligible for CPT	Stop CPT once TB treatment completed AND CD4 ≥25% (1-5 years old) or CD4 ≥200 cells/uL (≥5 years old), regardless of clinical stage

- Contraindications to CPT: Known or suspected hypersensitivity to Sulphonamides/ Trimethoprim
- Recommended doses as per weight (see table23)
- Common side-effects: Maculopapular rash/ hypersensitivity reaction - can be mild or severe
- (Stevens Johnson syndrome) - refer to experienced clinician for management.
- Dapsone can be used in patients with mild reactions to CPT. Recommended dose is 2 mg/kg/day or 4mg/kg/week. Do not use Dapsone if reaction was severe.

Table 23: Dosing table for Cotrimoxazole Preventive Therapy (CPT)

Age or Weight of Child	Dose	Suspension (200mg SMX / 40mg TMP 5ml	Single strength tablet (400mg SMX / 80mg TMP)	Double strength tablet (800mg SMX / 160mg TMP)
<6 months or <5kg	100mg SMX/ 20mg TMP	2.5ml	¼ tablet	-
6 months – 5 years or 5 – 15kg	200mg SMX/ 40mg TMP	5ml	½ tablet	-
6 – 14 years or 15 – 30kg	400mg SMX/ 80mg TMP	10ml	1 tablet	½ tablet
>14 years or >30kg	800mg SMX/ 160mg TMP	-	2 tablets	tablet

9.2 CPT in Adolescents & Adults on ART

Indications for CPT:

- CD4 <200 cells/uL
- Co-infection with TB
- Any WHO stage 2,3 or 4 condition
- CPT is safe to use in pregnancy and breastfeeding.
- Recommended dose of CPT: Cotrimoxazole 160/800mg daily
- Contraindications and side effects as per children (see above)
- Dosage adjustment in renal impairment:
- If eGFR10-50 mL/min: reduce dose to Cotrimoxazole 80/400mg daily
- If eGFR <10 mL/min: reduce dose to Cotrimoxazole 80/400mg three times per week
- Alternative to CPT: Dapsone 100mg daily for clients with mild hypersensitivity to Cotrimoxazole. **Do not use Dapsone if reaction was severe.**

10. CRYPTOCOCCAL SCREENING AND TREATMENT

10.1 Cryptococcal Prophylactic Treatment in Children & Adolescents <10 years old

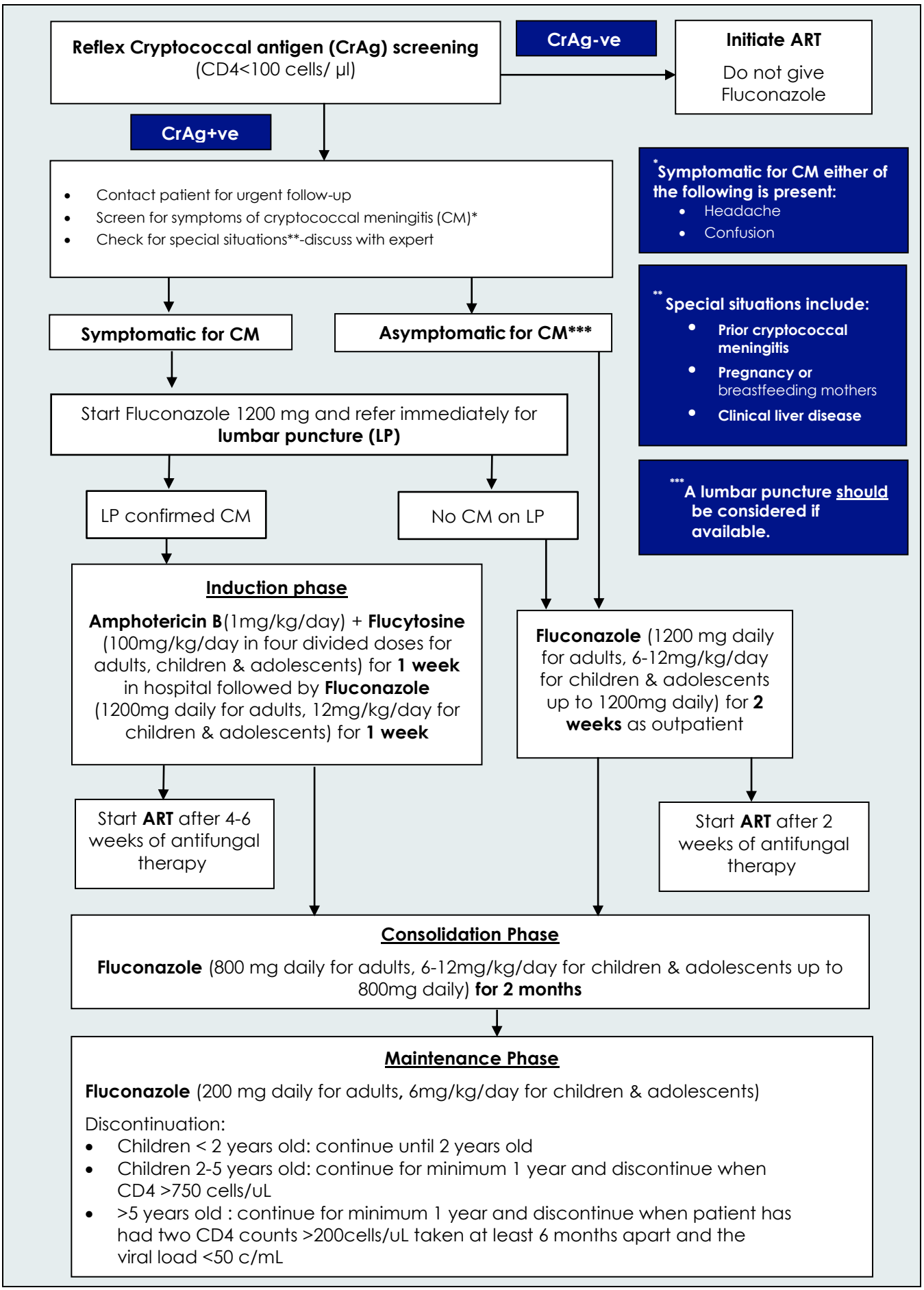
- Cryptococcal screening is not performed routinely in children and adolescents <10 years old
- Those who are diagnosed and treated for Cryptococcal Meningitis should continue prophylactic treatment while on ART as follows:
    - Children <2 years old must continue Fluconazole prophylaxis until they are 2 years old
    - Children 2-5 years old must receive Fluconazole prophylaxis for a minimum period of 1 year. Stop Fluconazole when CD4 >750 cells/mm³ on at least two occasions.
    - Children >5 years old must receive Fluconazole prophylaxis for a minimum period of 1 year. Stop Fluconazole when CD4 >200cells/uL on at least two occasions.

10.2 Cryptococcal Screening & Treatment in Adolescents ≥10 years old & Adults

- Cryptococcal meningitis (CM) is a serious opportunistic infection that can affect HIV-positive people with CD4 counts <100cells/µl.
- A reflex cryptococcal antigen test (CrAg) is performed by the laboratory on all specimens with CD4 <100 cells/ µl.
- Review reflex CrAg result with CD4 result of adolescents ≥10 years old & adults

- Management of patients with CrAg/ positive result (see figure 7)
- If symptoms of CM present-
    - Start Fluconazole 1200 mg daily and admit to hospital for a lumbar puncture (LP)
    - If CM is confirmed on LP, patients must be treated with an **induction phase** of intravenous Amphotericin B (1mg/kg/day) + oral Flucytosine (100mg/kg/day in four divided doses for adults, children & adolescents) given for **one week in-hospital**,
    - Followed by oral Fluconazole (1200mg daily for adults, 12mg/kg/day for children & adolescents up to maximum dose of 800mg) for one week,
    - Followed by a **consolidation phase** of Fluconazole (800 mg daily for adults, 6-12mg/kg/day for children & adolescents up to 800mg daily) for 2 months,
    - and then a **maintenance phase** of Fluconazole (200 mg daily for adults, 6mg/kg/day for children & adolescents).
    - Delay ART initiation by 4-6 weeks.
- If asymptomatic for CM or symptomatic patients with LP not suggestive of CM-
    - Give oral Fluconazole (1200 mg daily for adults, 6-12 mg/kg/day for children & adolescents) for 2 weeks as an outpatient,
    - Followed by a consolidation phase of Fluconazole (800 mg daily for adults, 6-12mg/kg/day for children & adolescents up to 800mg daily) daily for 2 months, then
    - a maintenance phase of Fluconazole (200 mg daily for adults, 6mg/kg/day for children & adolescents).
    - ART may be started **2 weeks** after initiation of Fluconazole prophylaxis.
- Pregnant women with CrAg positive **must** be referred for investigation with lumbar puncture (LP) on same day of diagnosis
- Precautions: Monitor ALT in patients on Fluconazole with clinical liver disease
- Patients with CrAg/CLAT negative result do not require Fluconazole prophylaxis and can be started on ART **immediately**.

Figure 7: Simplified Algorithm for Cryptococcal screening and treatment in adolescents and adults



11. REPORTING OF ADVERSE DRUG REACTIONS (ADR'S)

- Pharmacovigilance is an essential component of the ART programme which monitors the safety, efficacy and rationality of drug usage.
- The Medicines Control Council (MCC) defines an adverse drug reaction or adverse reaction as a response to a medicine that is noxious and unintended, including lack of efficacy, which occurs at any dosage and can also result from an overdose, misuse or abuse of a medication.
- All healthcare workers, including doctors, dentists, pharmacists, nurses and other professionals are encouraged to report all suspected adverse reactions to medicines, especially when the reaction is not in the package insert and is potentially serious of clinically significant
- All reports of ADR's are investigated and entered into a provincial database. This information is used to reduce the risks associated with ART and other medicines used in the ART programme and to improve the quality of patient care.

Consider the following factors when suspecting an ADR:

- What is the nature of the reaction?
- Did the reaction occur within a reasonable time to suggest a relationship to starting treatment with the suspected medicine?
- Is the reaction known to occur with the particular medicine a stated in the package insert or other reference?
- Did the patient recover when the suspected medicine was stopped?
- Did the patient take the medicine again after it had been stopped? If so, did the reaction occur again?
- Can this reaction be explained by other causes?

Report the following ADR's:

- All ADR's to newly marketed drugs or new drugs added to the EDL
- All serious reactions and interactions
- ADR's that are not clearly stated in the package insert
- All adverse reactions or poisonings to traditional or herbal remedies
- Report even if you are not certain that the medicine caused the event

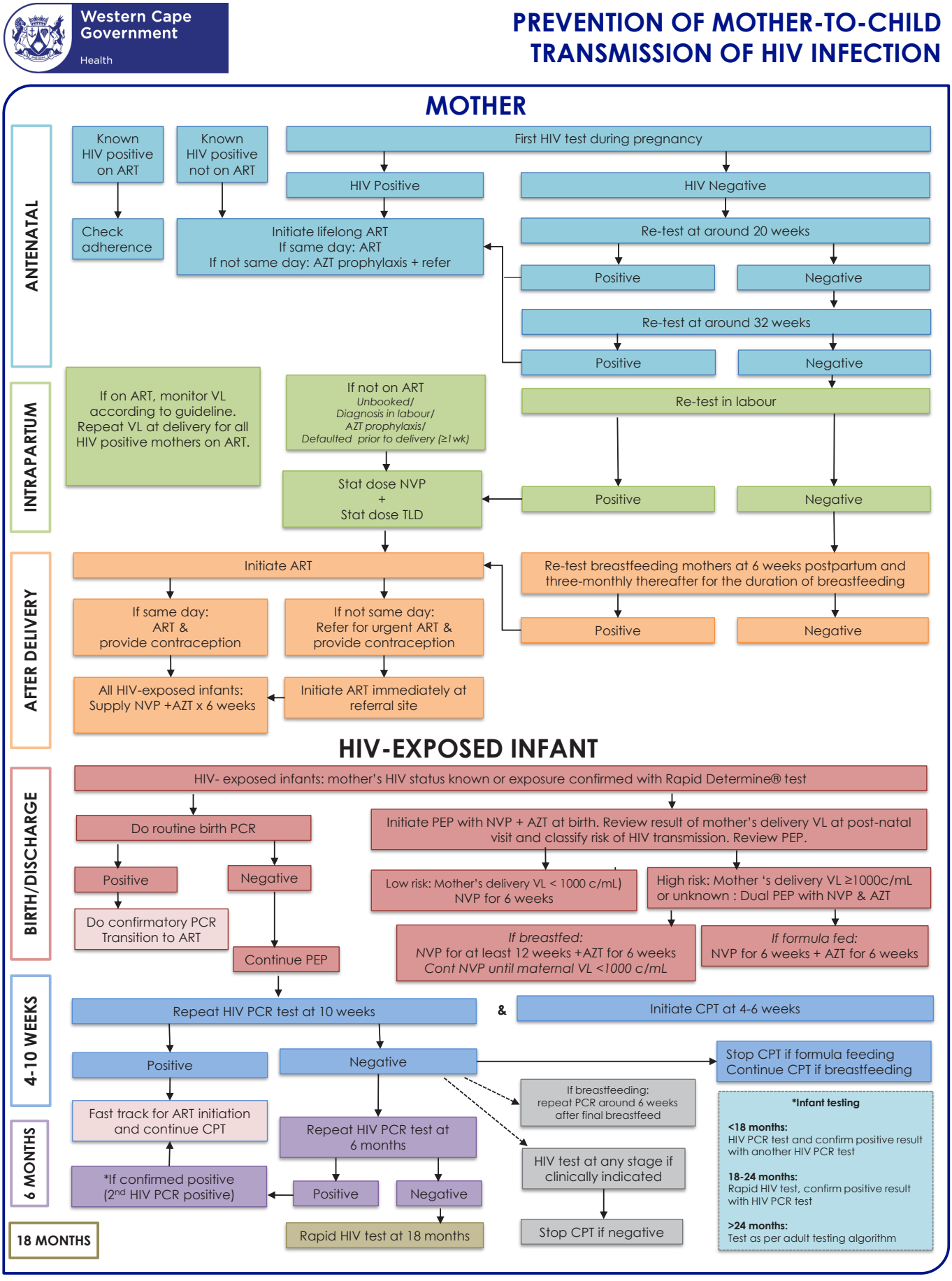
Report suspected product quality problems:

- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging or labelling
- Therapeutic failures

How to report an ADR:

- Fill in an adverse drug reaction/ product quality report form (refer to annexure 11) and submit to pharmacist for fowarding to the MIC Fax: 021 448 0503 | Email: jackie.jones@ uct. ac.za.
- The Western Cape Department of Health has developed a module, Adverse Drug Reactions, on the Provincial Central Repository, Sinjani, to capture this form electronically. Sinjani is accessible from any computer connected to the PGWC network: https://sinjani.pgwc.gov.za/live/. This link is also accessible under "Applications" on the Western Cape intranet: http://intrawp.pgwc.gov.za/Applications.asp

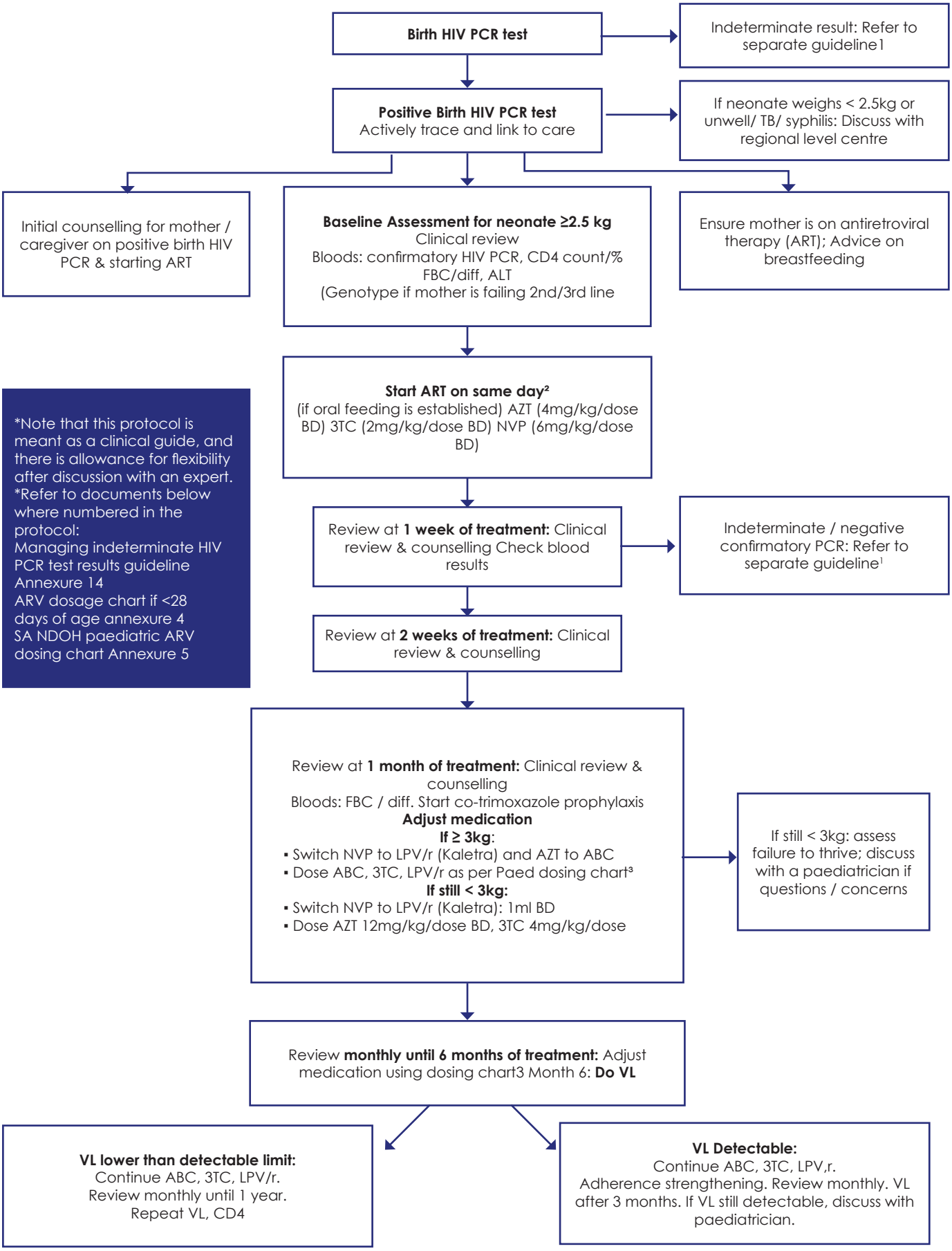
Annexure1: PMTCT Algorithm



Annexure 2: Neurodevelopmental Screening Tool for Children

DEVELOPMENTAL SCREENING			
	VISION AND ADAPTIVE	HEARING AND COMMUNICATION	MOTOR DEVELOPMENT
Always ask	Can your child see?	Can your child hear and communicate as other children?	Does your child do the same things as other children of the same age?
14 weeks	Baby follows close objects with eyes?	Baby responds to sound by stopping sucking, blinking or turning?	Child lifts head when held against Shoulder 
6 months	Baby recognises familiar faces	Child turns head to look for sound	Child holds a toy in each hand 
9 months	Child's eyes focus on far objects. Eyes move well together. (No squint)	Child turns when called	Childs sits and plays without support 
18 Months	Child looks at small things and pictures	Child points to 3 simple objects. Child uses at least 3 words other than names. Child understand simple commands	Child walks well  Child uses finger to feed
3 years	Sees small shapes clearly at 6 metres	Child speaks in simple 3 word sentences	Child runs well and climbs on things
5 – 6 years: School readiness	No problem with vision, Use a Snellen E chart to check	Speak in full sentences and interact with children and adults	Hops on one foot.  Able to draw a stick person.
REFER	Refer the child to the next level of care if child has not achieved the developmental milestone. Refer motor problem to Occupational Therapist/ Physiotherapist and hearing and speech problem to Speech Therapist/ Audiologist if you have the services at your facilities.		

Annexure 3: Algorithm for Initiation and Management of ART in Newly Diagnosed HIV-positive Infants <4 weeks old*



Annexure 4: ARV drug dosing chart for children <28 days of age and weighing ≥2.5kg 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**
≥ 2.5 - < 3	0.5 mL BD	5 mg BD	1 mL BD	10 mg BD	1.5 mL BD	15 mg BD
≥ 3 - < 4	0.8 mL BD	8 mg BD	1.5 mL BD	15 mg BD	2 mL BD	20 mg BD
≥ 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 (1ml, 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

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Department:
Health
REPUBLIC OF SOUTH AFRICA

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

	Abacavir (ABC)		Lamivudine (3TC)		Zidovudine (AZT)	Lopinavir/ritonavir (LPV/r)	Lopinavir/ritonavir when on Rifampicin (& for 2 weeks after stopping Rifampicin) Choose only one option:			#Atazanavir (ATV) + Ritonavir (RTV)	Dolutegravir (DTG)	Dolutegravir when on Rifampicin	Efavirenz (EFV)	
Target dose	8 mg/kg/dose **TWICE daily** **OR** **If ≥10kg**: 16 mg/kg/dose **ONCE daily**		4 mg/kg/dose **TWICE daily** **OR** **If ≥10kg:** 8 mg/kg/dose **ONCE daily**		180-240 mg/m²/dose **TWICE daily**	300/75 mg/m²/dose LPV/r **TWICE daily**	**LPV/r std dose + super-boosting with Ritonavir (RTV)** solution **TWICE daily** (≥0.75xLPV dose bd) **OR**	**LPV/r std dose + super-boosting with Ritonavir (RTV)** powder **TWICE daily** (≥0.75xLPV dose bd) **OR**	**Double-dose LPV/r tabs ONLY if able to swallow whole LPV/r tabs TWICE daily**	By weight band **ONCE daily**	By weight band **ONCE daily**	By weight band **TWICE DAILY**	By weight band **ONCE daily**	**Target dose**
Available formulations	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, 300 mg (not scored), FDC: AZT/3TC 300/150 mg	Sol. 80/20 mg/ml Adult tabs 200/50 mg Paed tabs 100/25 mg **TABLETS MUST BE SWALLOWED WHOLE**	Sol. 80 mg/ml	Oral powder 100 mg/packet	Adult tabs 200/50 mg, Paed tabs 100/25 mg	ATV caps 150, 200 mg; RTV tabs 100 mg **ATV CAPSULES AND RTV TABLETS MUST BE SWALLOWED WHOLE**	Tabs 50mg, FDC: TLD 300/300/50 mg	Tabs 50 mg	Caps/tabs 50,200, 600 mg; FDC: TEE 300/200/600 mg **TABLETS MUST BE SWALLOWED WHOLE**	**Available formulations**
Wt. (kg)	**Consult with a clinician experienced in paediatric ARV prescribing for neonates (<28 days of age) and infants weighing <3kg**													**Wt. (kg)**
3-3.9	2 ml bd		2 ml bd		6 ml bd	*1 ml bd	1 ml bd	100 mg (1 packet) bd	Do not use double-dose LPV/r tabs	Avoid ATV capsules when <15 kg or <6 years	Not currently recommended: dosing & formulations not available	Not currently recommended: dosing & formulations not available	Avoid using when <10 kg or <3 years	**3-3.9**
4-4.9														**4-4.9**
5-5.9	3 ml bd		3 ml bd			*1.5 ml bd	1.5 ml bd							**5-5.9**
6-6.9					9 ml bd									**6-6.9**
7-7.9	4 ml bd		4 ml bd		12 ml bd **OR** 1x100 mg tab bd									**7-7.9**
8-8.9														**8-8.9**
9-9.9														**9-9.9**
10-10.9	**Choose only one option** 6 ml bd **OR** 2x60 mg tabs bd	12 ml od **OR** 4x60 mg tabs od	**Choose only one option** 6 ml bd	12 ml od		**Choose only one option:** 2 ml bd **OR** 2x100/25 mg **paed tabs** am + 1x100/25 mg **paed tab** pm	1.5 ml bd		3x100/25 mg paed tabs bd				1x200 mg cap/ tab nocte	**10-10.9**
11-13.9														**11-13.9**
14-14.9	8 ml bd **OR** 2.5x60 mg tabs bd	5x60 mg tabs od **OR** 1x300 mg tab od **OR** 15 ml od	½x150 mg tab bd **OR** 8 ml bd	1x150 mg tab od **OR** 15 ml od	2x100 mg tabs am + 1x100 mg tab pm **OR** 15 ml bd	**Choose only one option:** 2.5 ml bd **OR** 2x100/25 mg **paed tabs** bd **OR** 1x200/50 mg **adult tab** bd	2 ml bd	200 mg (2 packets) bd	4x100/25 mg paed tabs bd **OR** 2x200/50 mg adult tabs bd	ATV 1x200 mg cap od + RTV 1x100 mg tab od	1x50 mg tab od	1x50 mg tab bd	1x200 mg cap/ tab + 2 x 50 mg caps/tabs nocte	**14-14.9**
15-16.9														**15-16.9**
17-19.9														**17-19.9**
20-22.9	10 ml bd **OR** 3x60 mg tabs bd	1x300 mg tab + 1x60 mg tab od	1x150 mg tab bd **OR** 15 ml bd	2x150 mg tab od **OR** 30 ml od	2x100 mg tabs bd **OR** 20 ml bd	**Choose only one option:** 3 ml bd **OR** 2x100/25 mg **paed tabs** bd **OR** 1x200/50 mg **adult tab** bd	2.5 ml bd							**20-22.9**
23-24.9		1x300 mg tab + 2x60 mg tabs od												**23-24.9**
25-29.9	1x300 mg tab bd	2x300 mg tabs od **OR** 1xABC/3TC 600/300 mg tab od	1x150 mg tab bd	2x150 mg tabs od **OR** 1xABC/3TC 600/300 mg tab od	1x300 mg tab bd **OR** 1xAZT/3TC 300/150 mg tab bd	**Choose only one option:** 3.5 ml bd **OR** 3x100/25 mg **paed tabs** bd **OR** δ1x200/50 mg **adult tab** bd + 1x100/25 mg **paed tab** bd	3 ml bd	300 mg (3 packets) bd	6x100/25 mg paed tabs bd **OR** 3x200/50 mg adult tabs bd				2 x 200 mg caps/tabs nocte	**25-29.9**
30-34.9						**Choose only one option:** 5 ml bd **OR** 4x100/25 mg **paed tabs** bd **OR** 2x200/50 mg **adult tabs** bd	4 ml bd	400 mg (4 packets) bd	8x100/25 mg paed tabs bd **OR** 4x200/50 mg adult tabs bd	ATV 2x150 mg caps od + RTV 1x100 mg tab od	1x50 mg tab od **OR** FDC: TLD if eligible od	1x50 mg tab bd **OR** FDC: TLD if eligible od + 50 mg 12 hours after TLD dose		**30-34.9**
35-39.9														**35-39.9**
≥40													1x600 mg tab nocte **OR** FDC: TEE if eligible od	**≥40**

* Avoid LPV/r solution in any full-term infant <14 days of age and any premature infant <42 weeks post conceptual age (corrected gestational age) or obtain expert advice.
δ Children weighing 25-29.9 kg may also be dosed with LPV/r 200/50 mg adult tabs: 2 tabs am + 1 tab pm.
Atazanavir + ritonavir should not be used in children/adolescents on treatment with Rifampicin, obtain expert advice. No dosage adjustments are required for children receiving treatment with Efavirenz and Rifampicin.

od = once a day; nocte = at night; bd = twice a day; am = in the morning; pm = in the evening; 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	10 ml or 1 tab	2 tabs od
Multivitamin Dose	2.5 ml od	2.5 ml od	5 ml od	10 ml od

Annexure 6: Dosing of 3rd line ARVs in Children & Early Adolescents

1. Darunavir (DRV) and Ritonavir (RTV)

- Formulations available:
  - Tablets: 75 mg, 150mg, 400mg, 600 mg
  - Oral suspension: 100 mg/mL (Not yet registered in SA, available on compassionate use access from manufacturer with MCC Sec 21 approval)
- Children <3 years of age OR <10kg: DRV is not recommended

Children ≥3 - <18 years of age AND ≥10 kg

Weight band (kg)	Dose of Darunavir and Ritonavir: administer doses in table below twice daily with food	Special considerations
10 - <11	DRV 200 mg (2.0 mL) + RTV 32 mg (0.4 mL)	Should only be used if patient is resistant to Lopinavir Children <3 years of age OR <10kg: DRV is not recommended
11 - <12	DRV 220 mg (2.2 mL) + RTV 32 mg (0.4 mL)	
12 - <13	DRV 240 mg (2.4 mL) + RTV 40 mg (0.5 mL)	
13 - <14	DRV 260 mg (2.6 mL) + RTV 40 mg (0.5 mL)	
14 - <15	DRV 280 mg (2.8 mL) + RTV 48 mg (0.6 mL)	
15 - <30	DRV 400 mg (1 x 400 mg tablet or 4 mL) + RTV 48 mg (0.6 mL) or 100 mg tablet if able to swallow whole	
30 - <40	DRV 475 mg (1 x 400 mg + 1 x 75 mg tablets or 4.7 mL) + RTV 100 mg tablet (or 1.25 mL if unable to swallow whole RTV tablet)	
≥40	DRV 600 mg (1 x 600 mg or 4 x 150 mg tablets or 6 mL) + RTV 100 mg capsule (or 1.25 mL if unable to swallow whole RTV tablet)	

Adolescent aged ≥18 years / adult dose: DRV 600 mg + RTV 100 mg both twice daily with food

- Adolescent (weighing ≥40 kg) and adult dose if treatment-naive or treatment-experienced with no darunavir resistance-associated mutations (V11I, V32I, L33F, I47V, I50V, I54L, I54M, T74P, L76V, I84V, and L89V): Darunavir 800 mg (2 x 400 mg tablets) plus ritonavir 100 mg once daily

2. Raltegravir (RAL)

- Formulations available:
  - Film-coated tablets: 400 mg
  - Chewable tablets: 25 mg, 100 mg (scored, dividable)
  - Note: Film-coated tablets and chewable are NOT interchangeable
  - Granules for oral suspension: single use packet of 100 mg RAL for suspension in 10mL water (10mg/mL) (Not yet registered in SA, available on compassionate use access from manufac-turer with MCC Sec 21 aproval)
- Dosing:
  - Neonatal dose (refer to Table below):
  - Birth – age 7 days: 1.5 mg/kg/dose once daily
  - **Note**: If the mother has taken RAL 2-24 hours before delivery, the neonate's first dose should be given between 24-48 hours after birth.
  - Aged 8-28 days: 3 mg/kg/dose twice daily

Body Weight (kg)	Dose of oral suspension
Birth to 1 Week - Once daily dosing*	
2 - <3 kg	**0.4 mL (4 mg) once daily**
3 - <4 kg	**0.5 mL (5 mg) once daily**
4 - <5 kg	**0.7 mL (7 mg) once daily**
1 to 4 Weeks - Twice daily dosing †	
2 - <3 kg	**0.8 mL (8 mg) twice daily**
3 - <4 kg	**1 mL (10 mg) twice daily**
4 - <5 kg	**1.5 mL (15 mg) twice daily**
***The dosing recommendations are based on approximately 1.5 mg/kg/dose.** **†The dosing recommendations are based on approximately 3 mg/kg/dose.**	

No dosing information is available for preterm infants or infants weighing <2 kg

- Infants ≥4 weeks of age: 6 mg/kg/dose twice daily (or dose according to Table below)
- Children ≥4 weeks of age AND weighing ≥3 kg - <20 kg: dosing of oral suspension:

Children ≥4 weeks of age AND weighing ≥3 kg - <20 kg: dosing of oral suspension

Weight band (kg)	Dose of Raltegravir	Special considerations
3 - <4	2.5 mL (25mg) twice daily	Film-coated tablets, chewable tablets and oral suspension are not interchangeable. Should only be considered for salvage therapy. Should not be added as the only active drug to a failing regimen. Can be used in children from 4 weeks and ≥3kg. Children can remain on oral suspension as long as their weight is < 20kg
4 - <6	3 mL (30 mg) twice daily	
6 - <8	4 mL (40 mg) twice daily	
8 - <11	6 mL (60 mg) twice daily	
11 - <14	8 mL (80 mg) twice daily	
14 - <20	10 mL (100 mg) twice daily	

Children with body weight 11-20 kg may be dosed with either oral suspension or chewable tablets.
Children ≥11 kg body weight:

- If <25 kg: chewable tablets by weight-based dosing chart below to maximum of 300 mg twice daily
- If ≥25 kg body weight, 400 mg film-coated tablet twice daily OR chewable tablets twice daily

Children: dosing of chewable tablets:

Weight band (kg)	Dose of Raltegravir	Number of chewable tablets
11 - <14	75 mg twice daily	3 x 25 mg twice daily
14 - <20	100 mg twice daily	1 x 100 mg twice daily
20 - <28	150 mg twice daily	1.5 x 100 mg twice daily
28 - <40	200 mg twice daily	2 x 100 mg twice daily
≥40	300 mg twice daily	3 x 100 mg twice daily

Child / adolescent with body weight ≥25 kg and adult dose: 400 mg film-coated tablet twice dai

3. Etravirine (ETR)

- Formulations available:

Tablets: 25 mg, 100 mg
- Children <6 years of age: not recommended
- Children ≥6 - <18 years of age AND ≥16 kg:

Children ≥6 - <18 years of age AND ≥16 kg:

Weight band (kg)	Dose of Etravirine	Special considerations
16 - <20	**100 mg twice daily**	**Should only be considered for salvage therapy** **Children <6 years of age: not recommended** **To be taken after a meal**
20 - <25	**125 mg twice daily**	
25 - <30	**150 mg twice daily**	
≥30	**200 mg twice daily**	

Adult dose: 200mg twice daily after food

4. Dolutegravir (DTG)

- Formulations available:
- Tablets: 10mg, 25 mg (not yet registered in SA), 50 mg ; (combination tablet containing tenofovir 300mg, lamivudine 300mg, dolutegravir 50mg; combination tablet containing abacavir 600mg, lamivudine 300mg, dolutegravir 50mg (available in private sector)
- Children <20kg: not recommended

Children ≥10 years of age AND ≥35 kg:

Weight band (kg)	Dose of Dolutegravir	Special considerations
Children > 20kg, adolescents and adults	**50mg once a day**	The fixed dose combination (TLD) can be prescribed for cleints ≥ 35kg ≥ 10 years Should be taken 2 hours before or 6 hours after taking cat-ion-containing antacids or laxatives, sucralfate, oral iron supplements, oral calcium supplements, or buffered medications **Dose adjustment required when with Rifampicin . Double DTG dose to 50mg 12-hourly. If on TLD fixed dose combination, add DTG 50mg 12 hours after TLD dose. Conitniue double DTG dose for 2 weeks after stopping rifampicin**

Annexure 7: Dosing of ARVs in Adolescents & Adults

ARV Dosing Guide for Late Adolescents & Adults		
Drug	**Standard Dose**	**Side-effects**
Nucleoside & Nucleotide Reverse Transcriptase Inhibitors (NRTI's)		
Abacavir (ABC)	300mg twice daily or 600mg daily	Hypersensitivity reaction (most common in first 6 weeks of therapy- do not rechallenge)
Tenofovir (TDF)	300mg daily	Nephrotoxicity
Lamivudine (3TC)	150mg twice daily or 300mg daily	Well tolerated, rarely pure red cell aplasia
Emtricitabine (FTC)	200mg daily	Hyperpigmentation(palms/soles)
Zidovudine (AZT)	300mg twice daily	Headache, nausea, neutropaenia, anaemia, lipoatrophy
Stavudine (d4T)	30mg twice daily	Peripheral neuropathy, lipoatrophy, hyperlactataemia
Non- Nucleoside Reverse Transcriptase Inhibitors (NNRTI's)		
Nevirapine (NVP)	200mg daily X14 days, then 200mg twice daily	Rash (including Stevens-Johnson syndrome), hepatitis
Efavirenz (EFV)	600mg at night (If <40kg, 400mg at night)	Rash, hepatitis, CNS effects, gynaecomastia
Etravirine (ETR)	200mg twice daily after meals	Rash, hepatitis
Protease Inhibitors (PI's)		
Lopinavir/ritonavir (LPV/r)	200/50mg tabs 2 tablets twice daily with food	Nausea, diarrhoea, dyslipidaemia
Atazanavir (ATV)	300mg daily plus ritonavir 100mg daily with food	Jaundice (due to unconjugated hyperbilirubinaemia), dyslipidaemia
Darunavir (DRV)	600mg twice daily plus ritonavir 100mg twice daily with food	Diarrhoea, nausea, rash, dyslipidaemia (low potential)
	800mg daily plus ritonavir 100mg dailywith food	Adolescents (>40kg) and adults with no darunavir resistance associated mutations on latest and previous genotypes (exclusion of DRV-RAMs: V11I, V32I, L33F, I47V, I50V, I54M, I54L, T74P, L76V, I84V and L89V)
Integrase Strand Transfer Inhibitors (InSTI's)		
Raltegravir (RAL)	400mg twice daily	Rash (including Stevens-Johnson), hepatitis, nausea, diarrhoea
Dolutegravir (DTG)	50mg daily	Headache, diarrhea, insomnia, weight gain

Annexure 8: Dosing of ARVs in Adults with Renal Impairment

ARV Dosing Guide for Adults with Renal Impairment		
Drug	Creatinine Clearance (CrCl)	
	10-50mL/min	<10mL/min
Nucleoside & Nucleotide Reverse Transcriptase Inhibitors (NRTI's)		
Stavudine (d4T)	15mg twice daily	15mg daily
Lamivudine (3TC)	150mg daily	50mg daily
Zidovudine (AZT)	300mg twice daily	300mg daily or 150mg twice daily
Tenofovir (TDF)	AVOID	
Abacavir (ABC)	No dose adjustment required	
NNRTI's Non- Nucleoside Reverse Transcriptase Inhibitors (NNRTI's)		
Efavirenz (EFV)	No dose adjustment required	
Nevirapine (NVP)		
Etravirine (ETR)		
Protease Inhibitors (PI's)		
Lopinavir / Ritonavir (LPV/r)	No dose adjustment required	
Atazanavir (ATZ)		
Darunavir (DRV)		
Integrase Strand Transfer Inhibitors (InSTI's)		
Raltegravir (RAL)	No dose adjustment required	
Dolutegravir (DTG)	No dose adjustment required	

Assessing Renal function				
	Age/Pregnancy Status	What must be measured?	Acceptable level for TDF use	Counahan Barratt formula eGFR (mL/min/1.73 m2) height [cm] x 40 = ---------- creatinine [µmol/L]
	≥10 and <16 years of age	eGFR using Counahan Barratt formula	>80 mL/min/1.73m²	
	Adults and adolescents≥16 years	eGFR using MDRD equation*	>50 mL/min/1.73m²	
	Pregnant women	Absolute creatinine level	<85 umol/L	

*The NHLS uses the MDRD formula to calculate creatinine clearance **for patients > 18 years** and reports eGFR. This is an acceptable approximation of creatinine clearance and can also be used.

Standard Laboratory Investigations for Children, Adolescents & Adults on ART

	Indicated	Before starting ART	M1	M2	M3	M4	M5	M6	M12	Annually thereafter
CD4	All clients	✓							✔	Repeat 6 monthly if last CD4<200
CrAg	If baseline CD4 <100cells/µL	✔								
RPR	All late adolescents & adults	✔								
Creatinine	If on TDF	✔	✔			✔			✔	✔
PAP smear	All adult women if >3 years since last PAP smear (do not delay ART start)	✔								Every 3 years unless abnormal previously
VL*						✔ (on 1st line regimens)		✔ (on 2nd or 3rd line regimens)	✔	✔
Hb and diff WCC	If on Zidovudine (AZT)	✔	✔		✔			✔		
ALT	If on Nevirapine	✔								
Fasting cholesterol and triglycerides	If on Lopinavir/ritonavir (Aluvia)				✔				only if abnormal previously	only if abnormal previously
HBsAg	before stopping TDF									

The above table shows the standard investigations for clients before and on ART – additional investigations might apply based on clinical investigations.
**not applicable to pregnant & breastfeeding women- see ART Guideline*

Annexure 10: Assessment of client with elevated VL ≥50 copies/mL

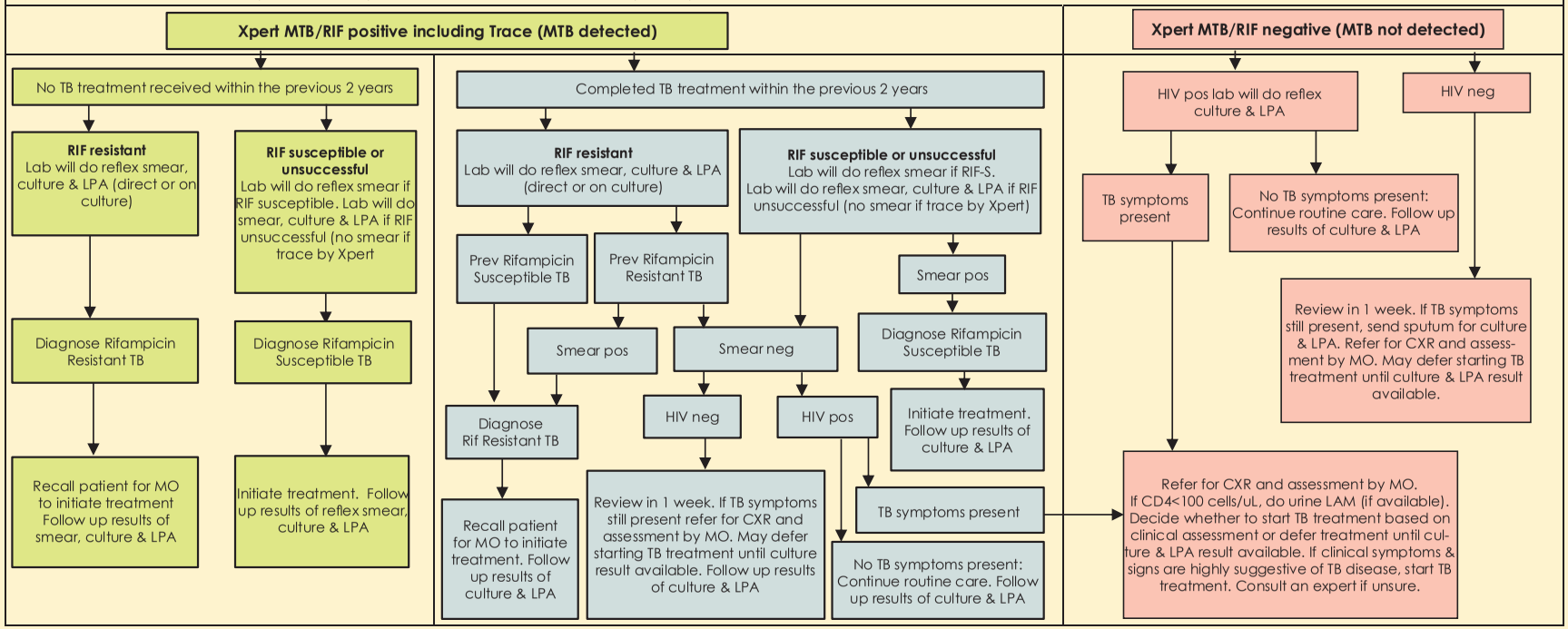
ASSESSMENT OF CLIENT WITH VIRAL LOAD ≥50 COPIES/ML		
A **Adherence**	Is adherence to medication poor? Ask about factors that may influence adherence e.g. • Medication side-effects, • Depression, • Alcohol or substance abuse, • Poor social support or • Non-disclosure. Pregnant women may experience nausea, heartburn, and constipation. Assess the need for symptomatic treatment with an anti-emetic, anti-diarrhea agent, or fiber supplement.	**Tips** Ask open ended questions e.g. "What makes it difficult for you to take your treatment?", and "How many doses have you missed this week?" Be non-judgmental. Statements like "we all miss a dose now and then" can encourage a client to be more open.
B **Bugs (Infections)**	Check for symptoms and signs of infection. Do a TB and STI screen.	Remember that immune compromised and pregnant clients may not exhibit overt symptoms of TB. If in doubt, do a TB GXP.
C **Correct Dose**	Is the client on the correct dose for his/her weight? This is especially applicable to young or malnourished clients who may have recently gained weight, or clients with previous renal impairment.	
D **Drug Interactions**	Are there any potential drug interactions? Consider: • Other prescribed treatment e.g. rifampicin, anti-epilepsy drugs • Over the counter treatment e.g. antacids • Supplements and herbal/traditional medications e.g. St John's wort	If in any doubt, call the **HIV Hotline** **0800 212 506**
E **RE-sistance**	Consider HIV drug resistance if other causes of virological failure have been excluded and the client is adherent to their medication. The need for 2nd-line ART is determined by current regimen and how long client has been on ART.	

Xpert MTB/RIF Ultra Diagnostic Algorithm for Pulmonary TB

- All clients entering a PHC facility must be screened for symptoms of TB [cough (≥2 weeks if HIV neg or any duration if HIV pos), recent loss of weight>1.5kg, fever > 2 weeks, night sweats]
- All clients who screen positive for 1 or more TB symptoms of pulmonary TB and are able to expectorate must have two sputum samples taken one hour apart and sent to lab for testing using Xpert MTB/RIF Ultra. If symptomatic and unable to expectorate or extrapulmonary TB suspected, refer for CXR and assessment by medical officer (MO).
- Universal TB testing must be done for all HIV positive pregnant women: send 2 sputum samples for Xpert MTB/RIF Ultra at first BANC visit regardless of whether or not TB symptoms are present. If asymptomatic and unable to expectorate, consider early morning sample collection or defer to following BANC appointment.
- Always do HIV test if status unknown, and repeat HIV test if previously tested HIV-ve >3 months ago
- If client is a healthcare worker, prisoner or close contact of DR-TB patient, or has completed TB treatment in previous 2 years request Xpert, smear, culture & LPA
- If client completed TB treatment in previous 2 years, a positive or trace Xpert MTB/RIF Ultra result may indicate live TB bacilli (active disease) or dead TB bacilli/DNA left over from the previous disease (not active disease now). The result of Xpert MTB/RIF Ultra must be considered along with all clinical information and advice may be sought from a TB expert if necessary
- Ask clients to return within 2 days for results of Xpert MTB/RIF Ultra and smear done on sputum specimen

Refer to Medical Officer urgently (same day) if:

- Breathlessness at rest or while talking
- Prominent use of breathing muscles
- Respiratory rate ≥ 30 breaths/minute, heart rate >120 beats per minute, BP < 90/60, temp>38°C
- Coughing up blood
- Confusion, agitation or unable to stand/walk unaided



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Annexure 12: Applications for 3rd Line ART Regimens

REQUEST FOR THIRD LINE ANTIRETROVIRAL THERAPY								
PATIENT DETAILS								
Patient First Name								
Patient Surname								
Date of Birth **Day/month/year**				**Patient number**				
Identity number				**Age**		**Gender**	**M/F**	
Weight (kg)		**BMI (kg/ m2)**		**Height (child)**				
FACILITY DETAILS								
Facility Name								
Authorised Prescriber								
Contact Number								
Email Address								
Date								
Signature of Authorised Prescriber								
Past medication history:								
Date started **Date stopped**	**Regimen**			**Reason for dis-continua-tion**	**Concurrent TB therapy**			
Reason for discontinuation codes: SE = Side effect, AL = Allergy, FC = Formulary change, NC = Non adherent								
Current regimen								
Has adherence been assessed? y/n What is the adherence level?								

Children: PMTCT history				
Was the mother on therapy during pregnancy or breastfeeding?				
What treatment did the mother take and for how long?				
as child breastfed?				
Did child receive any ARV at birth/after birth/ and during breastfeeding? State ARV and duration.				
CD 4 count			**Viral load**	
Last 3 CD 4 counts results:		**Children CD4%**	**Last 3 VL results:**	
Date:			**Date:**	
Date:			**Date:**	
Date:			**Date:**	
Laboratory Resistance test attached: y/n			**Results of Viral Resistance Test** **Date:**	
Most recent available tests:				
Hb (g/dL)				
ALT (U/L)				
Creatinine (µmol/L)				
Creatinine Clearance (mL/min/1.73 m2)				
White cell count (x 10^9/L)				
Neutrophil count (x 10^9/L)				
Hepatitis B status?				
Concomitant medication and indication				
Children: Is child able to swallow a tablet? y/n				
For office use only:				
Date received:				
Recommendation: **Date:**				

ADHERENCE TO TREATMENT ASSESSMENT FORM

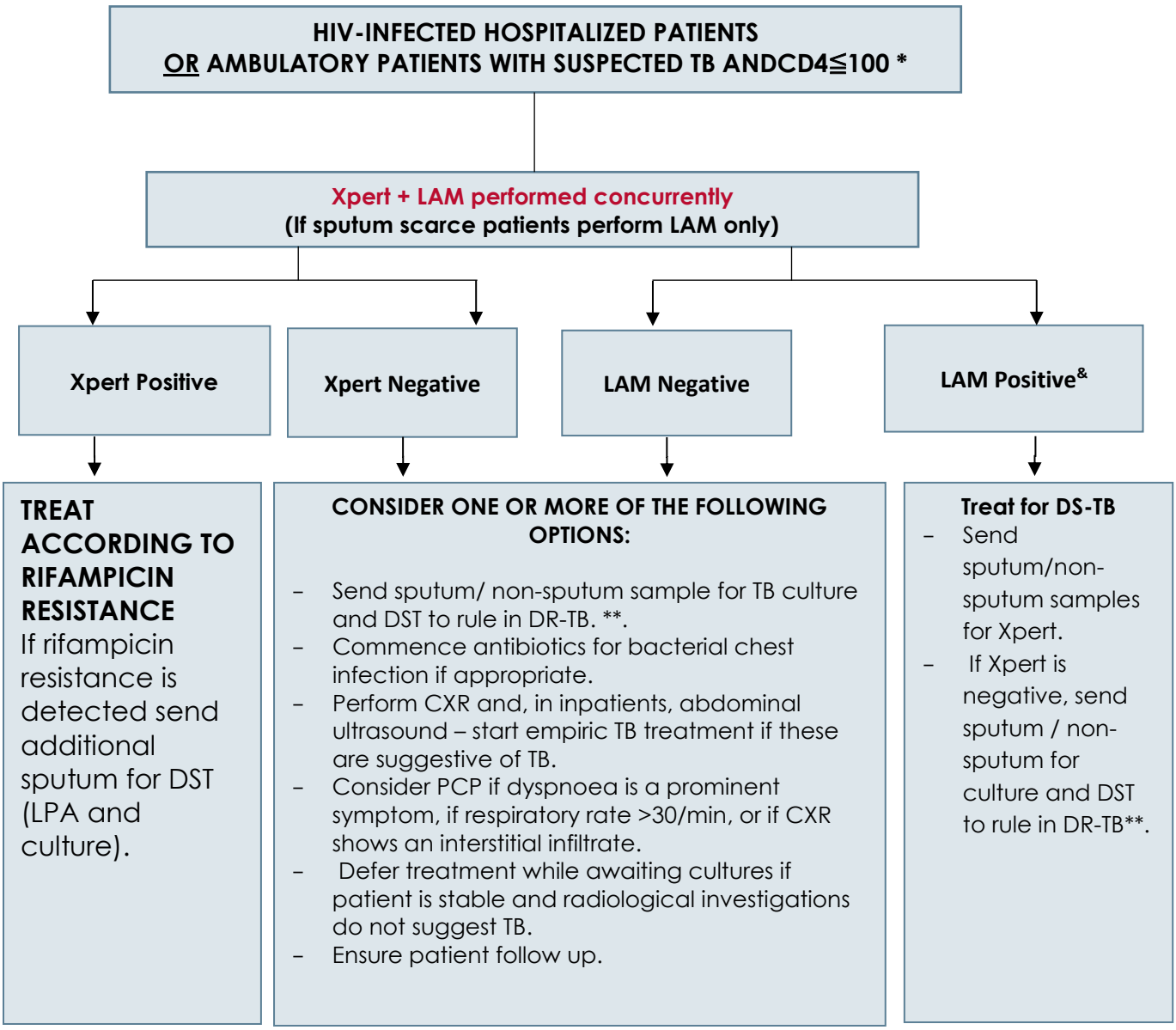
Patient name: _____ Clinician's name: _____
Date: _

Ask the client the following set of questions and make comments below each question. If the client is a child or adolescent, these questions need to be asked to the caregiver:

No.	Question
1.	**Explain how you take your ART – what time and how many tablets each time**
2.	**Have you forgotten to take your ART? If yes, how many doses have you missed since your last appointment?**
3.	**What were the reasons for you not remembering to take your ART? What do you do to remember to take your medication and not forget?**
4.	**What do you do when you miss a dose of your ART? Do you take the dose when you remember or wait until it's time for the next dose?**
5.	**Tell me 3 reasons why you want to adhere to your ART (why you take your tablets)?**
6.	**Have you disclosed your HIV status to someone? If so, do you have a treatment supporter?**
7.	**Do you have extra tablets stored in case you run out before you can go back to your clinic? What do you do if you plan to travel?**
8.	**How do you get to the clinic each month? Do you have a backup plan to get to the clinic if needed?**
9.	**Are you having any side effects from your tablets? Are you worried about taking your tablets?**
10.	**Are you taking any other medication? If yes, what are you taking and how many pills?**
11.	**Have you had problems swallowing your tablets, or do you vomit after taking the tablets? If yes, how often do you struggle to swallow the medication?**
12.	**How do you plan to make sure you take your ART if you use alcohol or drugs?**
13.	**Do you know what an undetectable viral load is? Do you know what a high viral load is? Why do you think your viral load is high?**

This adherence assessment tool must accompany the "Request for third line antiretroviral therapy" application form. If poor adherence is detected from the questions above, clinicians should increase tailored adherence support that assists the client in addressing the reasons for poor adherence.

Annexure 13: Algorithm for Use of Urine LF-LAM for diagnosis of TB in PLHIV



Annotations:
* LAM is indicated in hospitalized patients admitted to the medical wards (or seen in the emergency unit) with HIV stage 3 or 4 disease (suspicion of TB is not necessary and obtaining a CD4 count is not mandatory though the best yield is in with a CD4 ≤100). Patients with danger signs (respiratory rate >30 per minute, temperature >39°C, heart rate >120 beats per minute and unable to walk unaided) are most likely to be LAM positive, however, these signs are not necessary to initiate LAM testing.
In ambulatory patients LAM should only be requested when TB is suspected *and* CD4< 100 cells/ml. Thus, in an out-patient setting LAM should not be used in HIV uninfected persons or HIV-infected persons with a CD4> 100 cells/ml.
@ LAM should only be performed in children who can void urine i.e. non- catheter-based urine sample
** Culture and DST should be requested whenever biological samples can be obtained (if not initially available) and appropriate specialist consultation should be sought there is poor response to TB treatment.
& The LAM result must be read using the reference card supplied in the kit to minimise false positive and negative results.

Annexure 14: WC Adverse Drug Reaction Reporting Form

Patient Initials:			**DOB:**		**Gender:**	**Male**	**Female**
Weight (kg):		**Height (cm):**			**Starting CD4 (if HIV+) Current CD4 (if HIV+): Folder no:**		
Pregnant?	**Yes**	**No**	**Unknown**	**N/A**			
Treatment facility name:							
District/sub-district: **ICD 10 code(s) or disease(s):**							

List all medication patient was receiving at the time of the reaction including herbal, traditional and OTC medication

Medicine	**Dose**	**Date Started**	**Date stopped**	**Medicine**	**Dose**	**Date Started**	**Date stopped**

Anaemia requiring transfusion	**Hb:**	**Ototoxicity**	
Cholestatic hepatitis		**Pancreatitis**	
Congenital anomaly/ Pregnancy exposure/ foetal death		**Renal toxicity**	**Creatinine (µmol/L):**
Gynae com astia		**Skin reaction**	
Hypersensitivity reaction		**SJS/TEN**	
Hyperuricaem ia		**Sym ptom atic hyperlactataem ia** *(lactate>2 and symptoms)*	
Lactic acidosis (Metab olic acidosis and lactate>2mmol/L)		**Transam initis (gr 3=5-10XULN, gr 4>10XULN)/ symp hepatitis**	
Lipoatrophy	**(Fat loss)**	**Death**	
Lipohypertrophy (Abnormal fat accumulation)		**Suspected cause of death:**	
Neutropenia	**(Neutrophils less than 0.5 X 10□/L)**		
Other	**Describe:**		
Description of reaction:		**Date event started:**	
Investigations (including other relevant medical history):			
Management of adverse event:			

Died	**Recovered**	**Not yet recovered Hospitalised**	**Permanent dam-age/ disability**	**Regimen change - specify:**
Other outcome- specify:				

REPORTING DOCTOR / PHARMACIST / PROFESSIONAL NURSE							
Name:				**Qualifications:**			
Email:			**Tel:**		**Cell:**		
Signature:				**Date completed:**			
Please include additional information that you may deem necessary in your report (use additional paper)							
OFFICE USE ONLY: Database reference no:				**Submit to Manager: Pharmaceutical Services**			

Annexure 15: Management of Indeterminate HIV-PCR Results

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