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.

2015 (Amended Version)

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

Compiled by

Provincial Government of the Western Cape- Department of Health,

HIV/AIDS/STI/TB (HAST) Directorate

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The WC guidelines are based on 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 dated 24th December 2014

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 eligibility criteria for ART	Women within one year post-partum regardless of feeding choice or CD4 count. Children ≥5 years, adolescents and adults with CD4 ≤500 cells/mm^3. Adults with Hepatitis B infection, regardless of CD4 count. HIV-positive people in serodiscordant couples, regardless of CD4 count.
Initiation of ART in pregnant women	Initiate at any stage of gestation.
Closer monitoring of unsuppressed viral loads in third trimester of pregnacy	Viral load to be repeated after 1 month if unsuppressed in third trimester. Magnitude of log drops will be used to assess eligibilty to switch regimens.
Change in HIV-PCR testing schedule for HIV-exposed neonates	Routine HIV-PCR at birth for all HIV-exposed neonates, with repeat at 10 weeks if result is negative. PCR testing will no longer be done at 6 weeks.
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.
HIV testing in infants	Do HIV-PCR test at 18 weeks old if Nevirapine given until 12 weeks.
Change in indication for resistance testing in infants	Newly diagnosed infant < 2 years of age not on ART yet, whose mothers received PI-based ART during pregnancy and/or breastfeeding.
Baseline viral load testing in children & early dolescents newly diagosed with HIV no longer recommended	Viral load monitoring to start at month 4 after initiation of ART.
Monitor CD4 count annually in children<5 years	Routine monitoring until CD4 ≥500 copies/ml.
Phasing out of routine monitoring of CD4 counts in older children, adolescents and adults	CD4 counts to be monitored until one year after initiation of ART, then stopped if CD4 ≥200 copies/ml.
Abacavir to be used as alternative to Tenofovir in first-line regimens in late adolescents & adults with renal dysfunction	Motivation for the use of Abacavir is no longer required.
Monitoring of total cholesterol/ trigycerides on Lopinavir/ritonavir-based regimens	In children & early adolescents: at baseline then annually. In late adolescents & adults: at baseline, month 3, then annually only if clinically indicated.
Initiation of ART in patients with TB	Start within 2 weeks if CD4<50 (fast-track). Start between 2-8 weeks if CD4 ≥50. Start between 4-6 weeks if TB Meningitis present.
Includes section on IPT	Guidelines for the use of IPT in children, adolescents and adults.
Includes section on Cryptococcal screening and treatment	Updated guideline on Cryptococcal screening and treatment.

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Acronym glossary

3TC	Lamivudine
ABC	Abacavir
AIDS	Acquired Immune Deficiency Syndrome
ALT	Alanine Aminotransferase
ART	Antiretroviral Treatment
ARV	Antiretroviral
ATV/r	Atazanavir/ritonavir
AZT	Zidovudine
BMI	Body mass index
CD4	Cluster of Differentiation 4
CM	Cryptococcal meningitis
Cr	Creatinine
CrCl	Creatinine clearance
DDI	Didanosine
DRV/r	Darunavir/ritonavir
d4T	Stavudine
DNA PCR	DNA Polymerase Chain Reaction
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
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
TST	Tuberculin skin test
VL	Viral load
WHO	World Health Organization
WCC	White Cell Count

1. INTRODUCTION

1.1 Background

It has been just over a decade since the launch of the Antiretroviral Treatment (ART) Programme at public health facilities in South Africa (SA), and great progress has been made in terms of saving lives, extending life expectancy and preventing mother to child transmission of HIV. By 2012, nearly a third of the 6.5 million People Living with HIV (PLHIV) in SA had been exposed to ART[1]. This has contributed to SA's endeavour to reach the targets set by the Millennium Development Goals (MDG's) in 2000, aimed at reducing maternal mortality and combating HIV/AIDS[2].

In the global arena, there has been an ambitious shift in focus towards achieving eradication of the HIV epidemic. This concept is supported by evidence from research that ART is highly effective in treating HIV infection and preventing new infections in HIV-exposed individuals. Thus, in 2013, UNAIDS propagated the "90,90,90" targets, which are that by 2020, 90% of HIV-infected individuals should know their HIV status, 90% of those diagnosed with HIV should be receiving sustained ART, and 90% of individuals on ART should achieve virological suppression[3]. These targets have also been incorporated into the SA National HIV treatment programme.

The Western Cape HIV treatment programme is guided by the National Strategic Plan (NSP) (2012-2016)[4], which is evidence-based and focused on the drivers of the HIV epidemic in the country. Four strategic objectives form the basis of this approach to providing ART. These objectives relate to prevention and treatment of HIV, sustainment of health and wellness and protection of human rights and promotion of access to justice. It advocates for access to quality treatment, care and support services for people with HIV, STI's and TB.

The NSP identifies key population groups for HIV services. These groups are young women 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 recognises 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.

The new SA National ART and PMTCT guidelines of December 2014 have been consolidated to facilitate harmonisation of treatment across age groups and populations. Treatment regimens have been simplified to promote adherence and reduce side-effects. It has extended eligibility criteria for ART to include adults and children with CD4 <500, adults with Hepatitis B infection regardless of CD4 count and women within the first year post-partum regardless of feeding choice. The Western Cape programme is committed to reducing the incidence of new HIV infections, and is therefore extending its eligibility criteria further in this review to include HIV positive people in serodiscordant couples regardless of their CD4 counts (refer to Circular H214/2014).

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, MCH, SRH and Wellness
- Diagnose HIV earlier
- 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

1.3 Objectives

- Ensure timely initiation of ARVs for treatment and prevention according to the Presidential mandates
- Contribute to strengthening of the public and private health sectors' capacity to deliver high quality integrated health and wellness services
- Implement cascade management and ensure continuum of care
- Minimize unnecessary medicine toxicities
- Improve clinical outcomes, promote adherence and improve retention of patients in care
- Optimize the benefits of treatment as prevention by increasing ART coverage and encouraging annual HCT
- Simplify guidance for health workers to improve the quality of care for all PLHIV and HIV-exposed infants

1.4 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 extend eligibility criteria for initiation of ART to include PLHIV with CD4 ≤500 cells/ mm^3 and PLHIV with seronegative partners or Hepatitis B infection, irrespective of CD4 count
- To promote viral load testing as a preferred approach for monitoring ART success and diagnosing treatment failure
- To reinforce phasing out of Stavudine in first-line regimens
- 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

2. ART IN PREGNANT AND BREASTFEEDING WOMEN

2.1 HIV Testing During Pregnancy and Breastfeeding

HIV-infected women who are pregnant, breastfeeding or in the first year post-partum are eligible for lifelong antiretroviral therapy (ART). All newly diagnosed pregnant or breastfeeding clients with an unknown or previously negative HIV status **must** receive HIV Counselling and Testing (HCT) on the same day that they present to the healthcare facility. If they present with their partners, they may be offered couples HCT as an option, but this should not delay same-day testing.

Clients that are within one year post-partum should be offered HCT 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 the following intervals:

- 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 and have not been tested for HIV previously must be managed carefully. A full antenatal assessment and HCT must be done on the same day, and they should be referred to a medical officer if any abnormalities are detected.

2.2 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 babies. Known HIV-infected 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 table 1. 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) (see 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.

Table 1: Management of pregnant or breastfeeding clients who are newly diagnosed HIV-positive or known HIV-positive but not yet on ART

On Same Day as HIV Positive Diagnosis	At One-week Follow-up Visit
HIV and pre-ART counselling	HIV and ARV counselling
Adherence counselling	Adherence counselling
CD4 count	Review CD4 results: stop Cotrimoxazole prophylaxis if CD4 >200 and no TB.
Serum Creatinine + enquire about history of renal disease	Review Creatinine results If Serum Creatinine ≥85 (if pregnant) or CrCl <60ml/min (if breastfeeding): → Avoid Tenofovir, switch to Abacavir + Lamivudine + Efavirenz
WHO staging	Confirm WHO staging
TB symptom screening. If symptomatic, delay initiation of ART and refer for sputum test.	Review results of sputum test if done at previous visit. If no TB present, start ART. If TB present, refer for TB treatment and delay ART initiation for 2 weeks.
RPR and STI screening	STI screening, review RPR result. Treat if necessary.
Hb	Review Hb result.
Screen for chronic diseases	
If active psychiatric disorder present, start Zidovudine 300mg every 12 hours if Hb >8g/dl and refer urgently.	
If history of renal disease present, start Zidovudine 300mg every 12 hours if Hb >8g/dl and refer urgently.	
If no contraindications, no suspicion of TB and patient readiness confirmed, initiate ART with Tenofovir + Emtricitabine + Efavirenz as Fixed Dose Combination (FDC) If weight <40kg, adjust doses: Refer to annexure 5.	Monitor for side-effects of rash, dizziness, nausea, provide reassurance 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.	

Box 1: Management of clients testing HIV-positive during labour/delivery

- During labour or delivery, clients with no record of a previous HIV test result, or who have tested HIV negative during pregnancy, must be tested for HIV.
- If she tests HIV-positive, she will be eligible for ARVs.
- If she tests HIV-negative, the HIV test must be repeated 6 weeks post-partum.
- Give Nevirapine 200mg [sdNVP] stat + Truvada® [Tenofovir 300mg / Emtricitabine 200mg) stat + Zidovudine 300mg every 3 hours for the duration of labour
- Initiate Tenofovir + Emtricitabine + Efavirenz as Fixed Dose Combination [FDC] the next day if no contraindications and no suspicion of TB.
- Refer for ART counselling and adherence support.
- Schedule follow-up visit within one week.

2.3 Monitoring of Pregnant and Breastfeeding Women on ART

Close monitoring of Viral load (VL) is required in order to reduce the risk of HIV transmission to infants. Ensure that clients understand the purpose of regular VL monitoring. Algorithms for VL monitoring and management of unsuppressed VL's in pregnant and breastfeeding women are illustrated below in figure 1 and 2.

Monitor safety blood tests according to standard adult recommendations (refer to section 5.4).

2.3.1 Viral Load Monitoring During Pregnancy

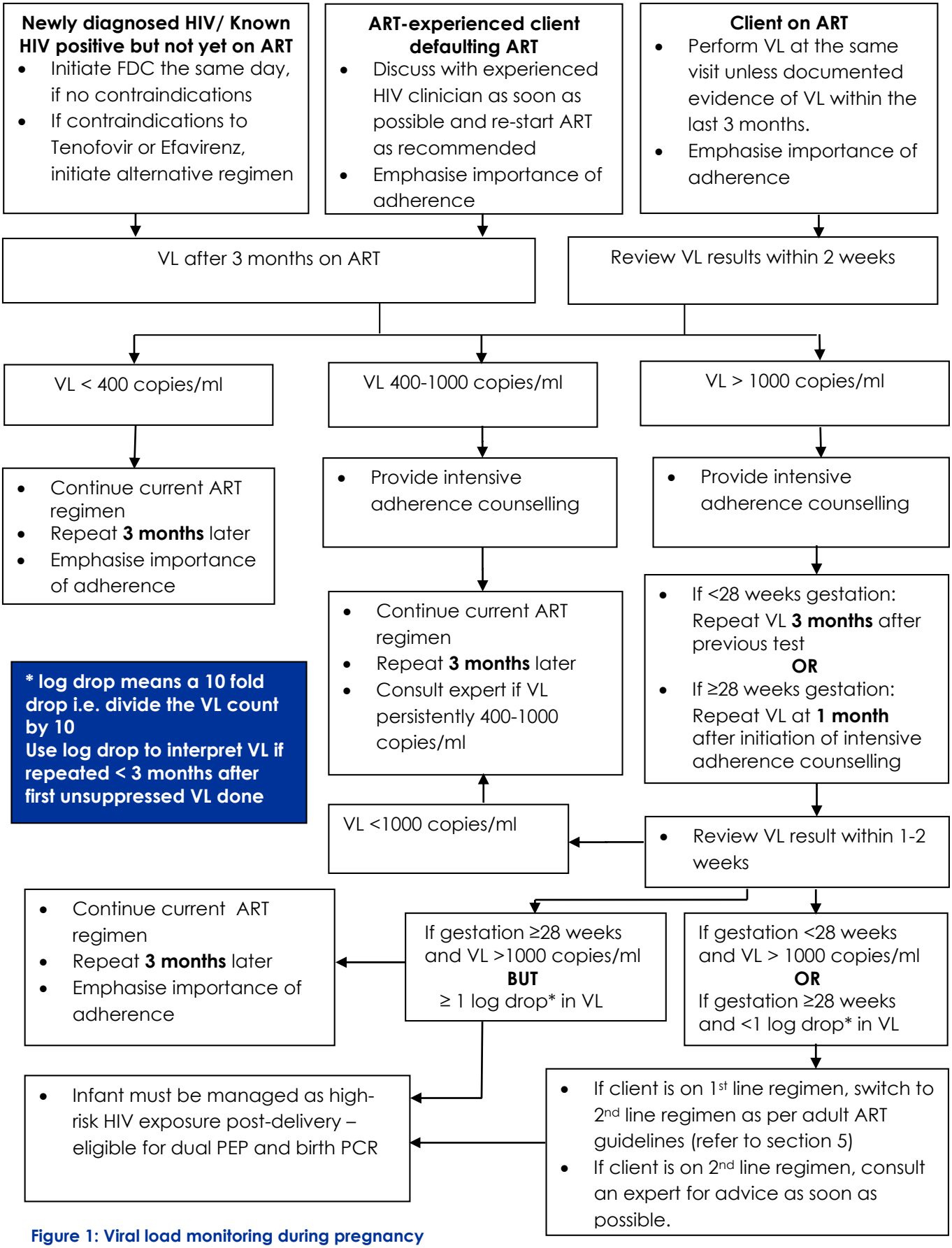


Figure 1: Viral load monitoring during pregnancy

2.3.2 Viral Load Monitoring During Breastfeeding

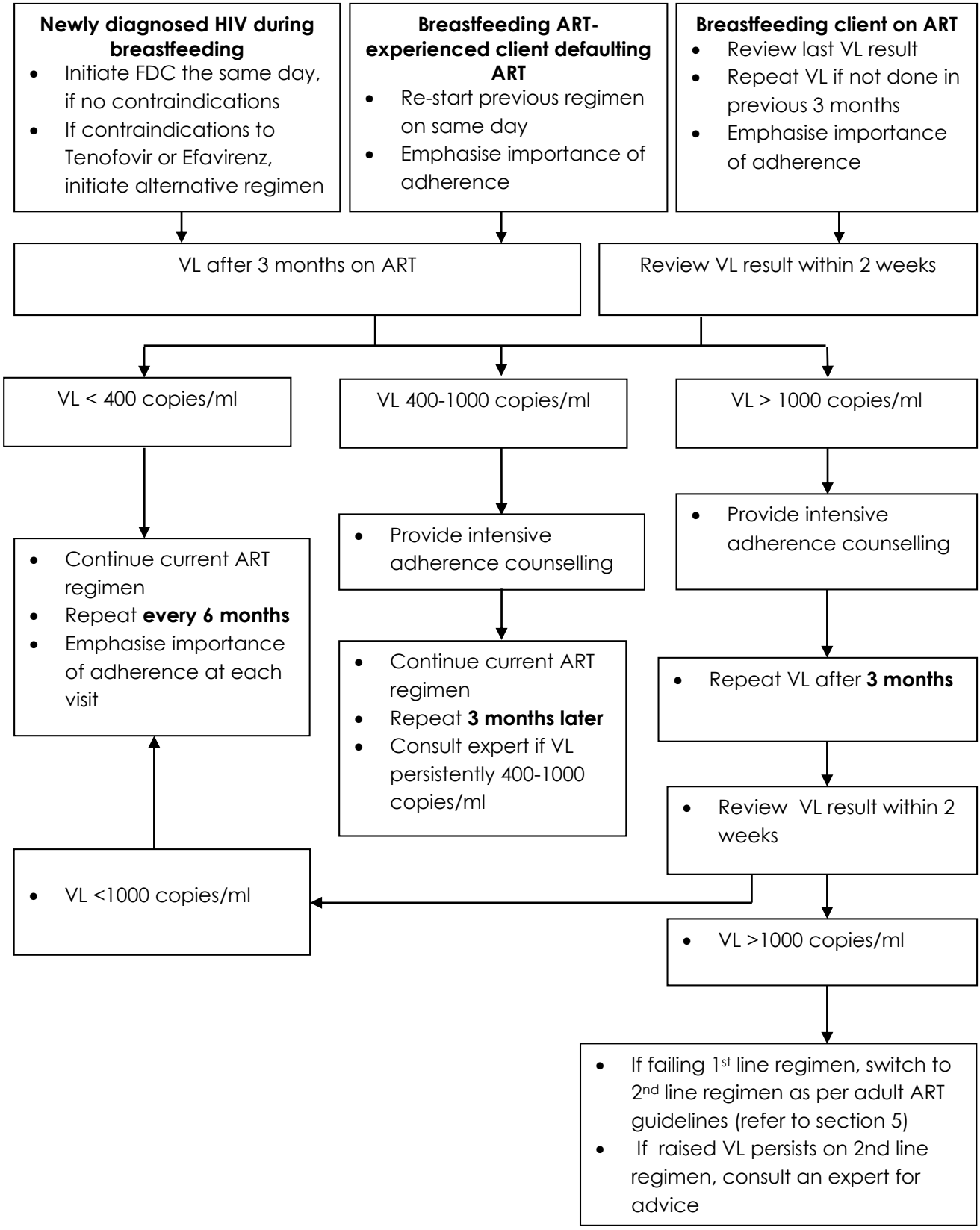


Figure 2: Viral load monitoring during breastfeeding

3. CARE OF THE HIV-EXPOSED INFANT

3.1 HIV Testing in HIV-exposed Infants

Infants of HIV-infected mothers may be at risk of acquiring HIV during the labour 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.

Table 2: 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** **(Do not use cord blood for PCR testing)**
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**
Around 18 weeks	Breastfeeding HIV-exposed infants who received NVP for 12 weeks then stopped **If NVP is extended beyond 12 weeks, do this test 6 weeks after final NVP*	HIV PCR test **If positive, confirm with a 2nd HIV PCR test**
At 9 months (immunization visit)	All HIV-exposed infants not on ART(irrespective of feeding choice)	Rapid HIV antibody screening test **If positive, do an HIV PCR test** **If positive, confirm with a 2nd HIV PCR test**
Around 18 months	All HIV-exposed infants not on ART (irrespective of feeding choice)	Rapid HIV antibody screening test If positive, confirm with rapid HIV antibody confirmatory test If results are indeterminate, do HIV ELISA 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 • Children considered for fostering 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:** **<9 months** HIV PCR test **If positive, confirm with a 2nd HIV PCR test** **9-<18 months** Rapid HIV antibody screening test. If positive, do an HIV PCR test **If positive, confirm with a 2nd HIV PCR test** **≥18 months** Rapid HIV antibody screening test **If positive, confirm with rapid HIV antibody confirmatory test** **If results are indeterminate, do HIV ELISA test**
6 weeks after final breastfeed	All HIV-exposed infants who were breastfed	**See Above**

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

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.

Table 3: Post-exposure prophylaxis (PEP) in HIV-exposed infants#

Subgroup of HIV-exposed infants	ARVs for PEP
1. Low risk of HIV transmission at birth: • Mother on ART with documented VL <1000 copies/ml <12 weeks before 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.
2. High risk of HIV transmission at birth: • Mother on ART with most recent VL ≥1000 copies/ml • Mother on ART with VL unknown <12 weeks before delivery** • Mother not on ART or initiated ART <12 weeks before delivery • Mother newly diagnosed HIV-positive during labour or <72 hours postpartum • Increased risk of HIV transmission during labour and delivery (irrespective of maternal VL) : o Clinical chorioamnionitis o Spontaneous preterm labour (<37 weeks gestation) o Prolonged rupture of membranes > 18 hours • 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 PCR at 10 weeks, around 18 weeks (6 weeks after stopping NVP) and 6 weeks after final breastfeed.
3. Increased risk of HIV transmission during breastfeeding*** • Mother on ART with most recent VL≥1000 copies/ml • Mother 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** *(Only stop NVP once maternal VL <1000 copies/ml. Provide intensive adherence support. If failing 1st line ART, repeat VL after 3 months. Switch to 2nd line ART if VL still >1000 copies/ml. If failing 2nd line ART, stop breastfeeding and manage according to adult ART guidelines.)* **Nevirapine daily for at least 12 weeks** **+** **Zidovudine twice daily for 6 weeks** *(Only stop NVP once maternal VL <1000 copies/ml.)* Start Cotrimoxazole prophylaxis if ≥4 weeks old. Do HIV PCR*. If positive, do confirmatory PCR and transition to ART. If negative, repeat PCR 6 weeks after stopping NVP and 6 weeks after final breastfeed.

#Refer to Tables 4, 5 & 6 for PEP dosing

*If result indeterminate, refer to Annexure 12 for further management.
**Do VL during labour or at delivery if possible- manage as low risk of transmission if VL<1000 copies/ml
***Applicable to infants ≤12 months old. Breastfeeding is not recommended >12 months if maternal VL is not suppressed. Consult a Paediatrician if further advice is required.

- 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 4 & 5 for dosing).
- Neonates who are nil per mouth (NPO) (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) will be required for prophylaxis during breastfeeding.
- **Transition infants who test HIV positive at birth from PEP to ART (refer to annexure 1).**
- **Fast track infants who test HIV positive at a later stage for ART (refer to section 4).**

Table 4: Oral dosing of Zidovudine for PEP in HIV-exposed infants

	Birth weight / gestational age	Age at exposure	Dosage
Zidovudine (AZT) syrup (10mg/ml)	If gestational age <35 weeks	Birth to 6 weeks	2 mg/kg/dose 12 hourly (0.2 ml/kg/dose 12 hourly)
	<3 kg and >35 weeks	Birth to 6 weeks	4 mg/kg/dose 12 hourly (0.4 ml/kg/dose 12 hourly)
	>3 kg and >35 weeks	Birth to 6 weeks	12 mg 12 hourly (1.2 ml 12 hourly)
	>3kg	>6 weeks	Dose according to weight-based dosing chart (2013)

Table 5: Oral dosing of Nevirapine for PEP in HIV-exposed infants

	Birth Weight	Age at exposure	Daily Dosage	Daily Volume
Nevirapine (NVP) syrup (10mg/ml)	<2.0kg	Birth to 2 weeks	2mg/kg	0,2 ml/kg
		2 to 6 weeks	4mg/kg	0,4 ml/kg
	2.0 – 2.5kg	Birth to 6 weeks	10mg	1ml
	>2.5kg	Birth to 6 weeks	15mg	1.5ml
	Age at exposure		**Daily Dosage**	**Daily Volume**
	*6 weeks to 6 months		20mg	2ml
	6 months to 9 months		30mg	3ml
	9 months to 12 months		40mg	4ml
***Consider dose of 4mg/kg if still an in-patient and weighs <2kg at 6-12 weeks. Also consider weight-based dosing if severely underweight for age at discharge.**				

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

Intravenous Dose of Zidovudine (AZT) (10 mg/ml in 200mg vial) Not a multi-dose vial. Prepare in sterile pharmacy for multiple doses.	≥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.		

3.3 Infant feeding

All pregnant women (HIV-positive, HIV-negative or with unknown HIV status) should receive at least 4 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 12 months of age, with appropriate complementary feeding whilst taking antiretroviral treatment as prescribed. Mothers must be counselled about the risks of mixed feeding (including the risks associated with the use of bottles, teats and pacifiers) their infants during their first six months of life, as exclusive breastfeeding reduces the risk of HIV transmission and improves child survival.

Mothers should also be intensively counselled about the importance of long-term adherence to ART and provided with adherence support where issues or barriers are identified. All HIV-exposed infants must be provided with prophylactic NVP alone or 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 2: 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 diarrhoea 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 tests 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.

Remind mothers that growth monitoring enables early intervention and it is very important to weigh HIV-exposed infants 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. ART IN INFANTS, CHILDREN AND EARLY ADOLESCENTS (10-15 YEARS OLD)

4.1 Eligibility 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 3. Those who are eligible should have developmental and clinical assessments, TB screening and 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 3). 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 3: Eligibility criteria for ART and fast-tracking of ART

Eligibility for starting ART
• All children less than 5 years of age: irrespective of CD4 or clinical staging • Children 5 years to 15 years: WHO clinical stage 3 or 4 **OR** CD4 ≤500 cells/ mm^3
Patients requiring fast tracking (i.e. start ART within 7 days of being eligible)
• Children less than 1 year of age • WHO clinical Stage 4 • MDR or XDR-TB • CD4 count ≤200 cells/mm^3 or ≤15%

4.2 Monitoring of Infants, Children & Early Adolescents on ART

Table 7: Monitoring of infants, children and early adolescents on ART

At initial Diagnosis of HIV	Purpose
Confirm HIV status	Ensure that Western Cape testing algorithm has been followed
Document weight, height, head circumference (<2yrs) and development	To monitor growth and development and identify eligibility for ART
Screen for TB symptoms	To identify TB/HIV co-infection
WHO Clinical Staging (≥ 5 yrs)	To determine if patient is eligible for ART
CD4 count	Children < 5 years: DO NOT wait for CD4 count to start ART
	Children ≥ 5 years: to determine eligibility for ART and Cotrimoxazole Preventive Therapy (CPT)(refer to section 8)
FBC + differential WCC	To detect anaemia; neutropaenia; thrombocytopaenia
Neurocognitive developmental assessments	With appropriate available tool (refer to annexure 2)
At Routine Follow-Up Visits for those not yet eligible for ART	**Purpose**
Document weight, height, head circumference (<2 years) and development	To monitor growth and development
Repeat CD4 count every 6 months	To determine if patient has become eligible for ART
WHO clinical staging	To determine if patient has become eligible for ART
ALT (if jaundiced or on TB treatment)	To assess for liver dysfunction
Neurocognitive developmental assessments	With appropriate available tool
Prior to initiation of ART	**Purpose**
FBC	If less than 8g/dl start ART and discuss with specialist
CD4 count (if not performed in last 6 months)	Baseline assessment
Cholesterol + Triglyceride if on PI-based regimen	Baseline assessment
ALT (if jaundiced or on TB treatment)	To assess for liver dysfunction
Neurocognitive developmental assessments	With appropriate available tool
On ART	**Purpose**
Height, weight, head circumference (<2yrs) and development	To monitor growth and developmental stages
Clinical assessment	To monitor response to ART and manage side effects
CD4: **All** at month 12 Then: Children <5 years: every 12 months Children >5 years: If CD4 < 200 cells/mm^3 repeat 6 monthly until > 200 cells/mm^3 If CD4>200 cells can stop monitoring routinely	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 - children <5 years: 6 monthly - children >5 years : every 12 months	To monitor virological response to ART To identify treatment failure and problems with adherence
Hb and differential WCC at month 1, 2, 3 and 6 months if on AZT	To identify Zidovudine-related anaemia
Cholesterol + Triglycerides at 1 year and then every 12 months if on PI-based regimen	To monitor for PI-related metabolic side-effects Advise dietary modification and refer for appropriate management if hyperlipidaemia present
Neurocognitive developmental assessments	With appropriate available tool (refer to annexure 2)

4.3 Standard ART regimens for Infants, Children & Early Adolescents

Table 8: Standard ART regimens for infants, children and early adolescents

1st Line Regimens*		
Neonates (infants <4 weeks old)	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 children under 3 years (or < 10kg)	Abacavir + Lamivudine + Lopinavir/Ritonavir	
Children ≥ 3 years (or ≥ 10kg): • NOT exposed to Nevirapine during PMTCT • EXPOSED to Nevirapine during PMTCT for 6 weeks or longer	Abacavir + Lamivudine + Efavirenz Abacavir + Lamivudine + Lopinavir/ritonavir Children who started on Abacavir + Lamivudine + Lopinavir/ritonavir before 3 years must remain on same regimen	
Weight < 40kg or age < 15 years	Abacavir + Lamivudine + Efavirenz	Nevirapine can be used if Efavirenz is contraindicated
Children on Stavudine	Change Stavudine to Abacavir if viral load <40 copies/ml If viral load >1000 copies/ml manage as treatment failure If viral load between 40 – 1000 copies/ml – consult expert for advice	
Children on Didanosine	Change all Didanosine to Abacavir regardless of VL	
2nd Line Regimen* (<15 years and <40kg)		
Failed 1st line NNRTI based regimen		
First line NNRTI-based regimen:	**Recommended second line regimen:**	
Abacavir + Lamivudine + Efavirenz (or Nevirapine)	Zidovudine + Lamivudine + Lopinavir/ritonavir	
Stavudine + Lamivudine + Efavirenz (or Nevirapine)	Zidovudine + Abacavir + Lopinavir/ritonavir	
Failed 1st Line Protease Inhibitor (PI) based regimen		
Abacavir + Lamivudine + Lopinavir / ritonavir	Should be managed as for third line regimens - see section below.	
Stavudine + Lamivudine + Lopinavir/ritonavir		
Unboosted PI-based regimen		
Rifampicin while on Lopinavir/ ritonavir		
3rd Line Regimens*		
Failing any 2nd line regimen (see WC *circular H158/2014*)	Should be managed by a Paediatric Infectious Disease Specialist on the basis of genotype resistance testing Indications for resistance testing: • 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. • Patients on a PI regimen with virological non-suppression defined as at least three viral load measurements of ≥1000 copies/ml (≥log 3) at least 8-12 weeks apart after adherence has been addressed. o Children (<15 years of age): receiving PI regimen for at least 1 year	

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

4.4 Transition from Paediatric/ Early Adolescent ART regimens to Late Adolescent/ Adult ART regimens

Late adolescents with an undetectable VL (<40 copies/ml) and no side-effects on Abacavir + Lamivudine + Efavirenz, can remain on the same regimen until they become eligible for Tenofovir + Emtricitabine + Efavirenz (provide as Fixed Dose Combination [FDC]) at 15 years old **and** weight ≥ 40 kg.

- When an adolescent with an undetectable VL (within the last 8 weeks) reaches 15 years and 40 kg, a creatinine clearance (CrCl) and urine dipstix should be performed
  The Schwartz formula should be used to calculate CrCl if
  <16 years:
  $$CrCl = \frac{\text{height [cm]} \times 40}{\text{creatinine [µmol/l]}}$$
- If the CrCl is >80 and no proteinuria on urine dipstix, then the patient must be switched to FDC (TDF + FTC + EFV).
- If the CrCl is <80 or >1+ Proteinuria on urine dipstix then refer to an expert for advice before switching.
- If the HIV VL is between 50-1000 copies/ml, consult an expert for advice.
- If the HIV VL is >1000 copies /ml, exclude non-adherence then treat as virological failure.

5. ART IN LATE ADOLESCENTS (15-19 YEARS OLD) AND ADULTS

5.1 Eligibility Criteria and Timing of Initiation of ART

Box 4: Eligibility criteria for ART and fast-tracking in late adolescents & adults

Eligibility for starting ART
• CD4 count (≤500) cells/mm³ irrespective of WHO clinical stage **OR** • Irrespective of CD4 count o All types of TB o HIV positive women who are pregnant, breast feeding or within one year post-partum (irrespective of feeding choice) o WHO stage 3 or 4 o HBV co-infection o HIV positive partner in a serodiscordant couple • Prioritise those with CD4 ≤350 cells/mm³ or advanced HIV disease

Patients requiring fast tracking	
HIV positive women who are pregnant or breast feeding **OR** Patients with a CD4 ≤ 200 **OR** Patients with WHO stage 4 disease **OR** Patients with TB/HIV co-morbidity with a CD4 < 50	Where capacity exits: initiate **SAME day** as eligibility established (otherwise within 7 days) Within **7 days** Within **7 days** Within **2 weeks** of commencement of TB treatment

Box 5: Management of patients with CD4 >500 and not yet eligible for ART

- Transfer to a wellness programme for regular follow-up and repeat CD4 count every 6 months.
- Advise how to avoid HIV transmission to sexual partners and children.
- Perform TB screening at every visit and initiate IPT if eligible.
- Provide counselling on nutrition and healthy lifestyle.
- Do Pap smear for women at diagnosis, and repeat every 3 years if no abnormalities detected.
- Screen for and manage sexually transmitted infections (STI's).
- Provide support for disclosure and partner notification. Discuss the option of couples counselling and HCT for partner.
- Provide information and counselling related to fertility, including planning for conception or contraception as needed.
- Screen for and manage co-morbidities and non-communicable diseases
- Encourage patients to return whenever they have health problems

5.2 Initiation of ART in HIV Positive Partners in Serodiscordant Couples

Box 6: Rationale and approach to ART in serodiscordant couples

Rationale for 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[5]. • 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 HCT should be offered the option of couples HCT. • 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 HCT. If unavailable, make effort to test the partner as soon as possible and offer the option of couples HCT 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 be offered ART if the pregnant/ breastfeeding patient's HIV test is negative. • All patients who test HIV-positive after HCT should receive post-test counselling with support for disclosure to their partners. They should then be offered couples counselling followed by HCT for 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 HCT for the HIV-negative partner every 6 months. • Patients eligible for ART due to being in an HIV serodiscordant couple should be commenced on lifelong ART according to the standard adult protocol. • Patients on ART and their partners should be encouraged to access available health services for TB screening, treatment of STI's, family planning and conception counselling.

5.3 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 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 possible.

5.4 Monitoring of Late Adolescents & Adults on ART

Table 9: 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: • ART (CD4 ≤500) • fast-tracking (CD4 ≤200/ stage 4) • prioritisation (CD4 ≤350) • Cotrimoxazole prophylactic treatment (CPT) (CD4 < 200)(Refer to section 8) • CrAg or CLAT (CD4 < 100)(Refer to section 9)
Screen for pregnancy or ask if planning to conceive	To identify pregnant women eligible for ART, opportunity to offer appropriate family planning/ conception counselling
Screen for TB symptoms	To identify TB/HIV co-infection (refer to WC TB screening tool - annexure 8)
Mantoux test (TST)	Assess need for IPT
Screening for STI's and syphilis	To manage STI's and provide counselling on prevention of STI's and condom use
Assessment of major non-communicable diseases	To identify any concomitant chronic disease
Screen for Hepatitis B if CD4 >500	To identify HBV co-infection and eligibility for ART
Weight and Height in adolescents	To determine appropriate ART regimen
At Routine Follow-Up Visits for those not yet eligible for ART	**Purpose**
Repeat CD4 count and clinical staging every 6 months	To determine eligibility for ART
Screen for TB symptoms at every visit to identify TB suspects Offer IPT if no TB symptoms (refer to section 7)	To identify TB/HIV co-infection To treat latent TB infection

Prior to initiation of ART	Purpose
CrAg/CLAT: If baseline CD4<100 cells/mm³	To identify patients who require treatment or prophylaxis for Cryptococcal Meningitis (CM) (refer to section 9)
Serum creatinine for clients initiating on Tenofovir	To detect renal insufficiency- calculate creatinine clearance (CrCl) as shown below: If < 16 years: the following formula should be used: $\text{CrCl [ml/min]} = \frac{\text{height [cm]}}{\text{serum creat [µmol/l]}} \times 40$ If ≥ 16 years, use adult weight-based formula: $\text{CrCl [ml/min]} = \frac{(140 - \text{age})}{\text{serum creat (µmol / l)}} \times \text{Wt (kg)}$ Females: multiply CrCl by 0.85 In adolescents <16 years: DO NOT use Tenofovir if CrCl ≤80. In adults/ adolescents ≥16 years: DO NOT use Tenofovir if CrCl ≤ 50. If the CrCl is abnormal: Check urine dipstix for proteinuria and repeat serum creatinine after 1 month. Refer to experienced clinician if renal dysfunction persistent. In pregnant women : DO NOT use Tenofovir if serum creatinine ≥ 85 µmol/l Refer to section 5.5 for alternate regimens. Doses of ARV's may need to be adjusted for renal impairment. Refer to annexure 6.
Hb and differential WCC: for clients initiating on Zidovudine	To detect anaemia/neutropaenia Do not use AZT if Hb ≤ 8 g/dl
ALT: for clients initiating on Nevirapine	To detect liver dysfunction
Fasting cholesterol and triglycerides for clients initiating Lopinavir/ritonavir	To identify clients with contraindications to LPV/r or at risk of LPV/r related hyperlipidaemia. If total cholesterol >6mmol/L or triglycerides >5mmol/l, consider using Atazanavir/r instead of LPV/r.

On ART	Purpose
CD4 at month 12 If CD4 < 200 cells/mm³ repeat annually until > 200 cells/mm³ then stop monitoring CD4 routinely. If CD4 >200 cells/mm³ stop monitoring CD4 routinely.	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 400-1000 copies/ml, repeat after 6 months. If unchanged, consult a specialist for advice. If VL >1000, repeat within 3 months (2 months after adherence intervention). If second VL >1000 copies/ml, manage as virological failure (refer to section 5.6) If pregnant or breastfeeding, refer to PMTCT guideline (section 2) for VL monitoring	To monitor response to treatment and detect treatment failure 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 Tenofovir	To detect TDF toxicity- calculate CrCl (see formulae above)
ALT: If on Nevirapine or Efavirenz and develops rash or symptoms suggestive of hepatitis If on TB treatment and Lopinavir/ritonavir	To detect 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.
HB and differential WCC: at month 1, 2, 3 and 6 if on Zidovudine	To detect Zidovudine toxicity
Fasting cholesterol and triglycerides at month 3 on Lopinavir / ritonavir. 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 should include dietary modification and statins if indicated, refer to doctor.
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.

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

Table 10: Standard 1st line ART regimens for late adolescents & adults

1st Line Regimens*		
Indications	**Regimen**	**Comments**
Initiation of ART in pregnant or breastfeeding women, late adolescents and adults	Tenofovir **+** Emtricitabine (or Lamivudine) **+** Efavirenz *Provide as fixed dose combination*	Use TDF in adolescents only if ≥15 years old **AND** ≥40kg **AND** CrCl ≥ 80 (see section 5.4 for formula to calculate CrCl)
Contraindications to Tenofovir	Abacavir **+** Lamivudine **+** Efavirenz	Renal disease (CrCl ≤ 50 ml/min in adults or CrCl <80ml/min in late adolescents) Concurrent use of other nephrotoxic drugs e.g. aminoglycosides (Kanamycin) for MDR-TB Pregnant women: Cr > 85µmol/l **No motivation required**
Contraindications to Tenofovir and Abacavir	Zidovudine **+** Lamivudine **+** Efavirenz	Renal disease [CrCl ≤ 50 ml/min] or the concurrent use of other nephrotoxic drugs e.g. aminoglycosides (Kanamycin) and hypersensitivity to Abacavir
Contraindications to Tenofovir , Abacavir and Zidovudine	Stavudine **+** Lamivudine **+** Efavirenz	Renal disease [CrCl ≤ 50 ml/min] or the concurrent use of other nephrotoxic drugs e.g. aminoglycosides (Kanamycin), hypersensitivity to ABC and severe anaemia (Hb ≤ 8 g/dl)
Currently on Stavudine -based regimen	Tenofovir **+** Emtricitabine (or Lamivudine) **+** Efavirenz or Nevirapine	Switch to Tenofovir-based regimen if virologically suppressed and CrCl >50ml/min. If CrCl reduced, consider substitution with Abacavir. If VL >1000copies/ml, manage as virological failure and consider switching to 2nd line regimen
Contraindications to Efavirenz	Tenofovir **+** Emtricitabine (or Lamivudine) **+** Nevirapine **OR** Lopinavir/ritonavir	Psychiatric co-morbidity or intolerance to Efavirenz e.g. shift workers. Patients should **not** be initiated on NVP if: - Female with an initial CD4 > 250 cells/mm^3 - Males with an initial CD4 > 400 cells/mm^3 - Use Lopinavir/ritonavir instead
Late adolescents ≥15 years with weight <40kg	Abacavir **+** Lamivudine **+** Efavirenz	If adolescent weight <40kg, align with paediatric regimen **No motivation required**

***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.**

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

- Virological failure in a patient on a 1st line regimen is diagnosed when VL>1000 copies/ml on two separate occasions 2-3 months apart. This is an indication to switch to a 2nd line regimen.
- If a patient is on a Tenofovir and Lamivudine /Emtricitabine based regimen, check Hepatitis B status 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 and Lamivudine/Emtricitabine in the new regimen until Hepatitis B status is known.
- The choice of ARV's in the 2nd line regimen will depend on composition of the 1st line regimen- refer to table 11.

Table 11: Standard 2nd line ART regimens for late adolescents & adults

2nd Line Regimens*		
Indications	**Regimen**	**Comments**
Failing on Tenofovir -based regimen with HBsAg positive	Tenofovir + Zidovudine + Lamivudine/ Emtricitabine + Lopinavir/ ritonavir	
Failing on Tenofovir - based regimen with HBsAg negative	Zidovudine + Lamivudine + Lopinavir/ ritonavir	
Failing on Abacavir- based regimen	Zidovudine + Lamivudine + Lopinavir/ ritonavir	
Failing on Tenofovir or Abacavir-based regimen with contraindication to Zidovudine	Stavudine + Lamivudine + Lopinavir/ ritonavir	Severe anaemia (Hb ≤ 8 g/ dl)
Failing on a Stavudine- or Zidovudine-based regimen	Tenofovir + Lamivudine/ Emtricitabine + Lopinavir/ ritonavir	
Failing on a Stavudine- or Zidovudine-based regimen with contraindication to Tenofovir	Abacavir + Lamivudine + Lopinavir/ ritonavir	Renal disease [CrCl ≤ 50 ml/min] or the concurrent use of other nephrotoxic drugs e.g. aminoglycosides (Kanamycin) **No motivation required**
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	**No motivation required** Advise dietary modifications and refer to doctor.

***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.**

5.7 3rd Line Drug Regimens for ART in Late Adolescents & Adults

If a patient has virological failure on a 2nd line regimen, a decision to switch to a 3rd line 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) do not have PI resistance mutations. The provision of 3rd line drugs will be limited to patients with intermediate or high level PI resistance on genotyping. Resistance testing will only be offered to patients with good adherence, assessed objectively by means of pharmacy scripting refills and the completed adherence evaluation form, submitted along with the application.

Indications for resistance testing in adults and adolescents:

- Patients on a PI regimen with virological non-suppression defined as at least **three** viral load measurements of ≥1000 copies/ml (≥log 3) at least 2-3 months apart, and
- Must be receiving PI regimen for at least 2 years

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

***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.**

5.8 Indications for Referral to a Medical Officer

- Baseline creatinine clearance less than 50 ml/min, with no improvement after one month
- Increase in serum creatinine after initiation of Tenofovir
- Decrease in Hb after initiation of Zidovudine
- Poor response to TB treatment or suspicion of IRIS
- Change in clinical stage of disease while on ART
- Clinical signs of possible meningitis: e.g. confusion; headaches
- Psychiatric illness

5.9 Family Planning and Reproductive Choices for Patients on ART

Discuss contraceptive and conceptive options with all clients on ART. Advocate for the use of dual protection if no pregnancy is planned.
For women planning a pregnancy:

- Enquire about the HIV status of the partner - if unknown, advise HCT and offer couple's counselling. If partner is HIV-positive, refer him to doctor to optimise HIV management.
- Check patient's general health, review WHO stage and latest blood test results.
- Screen for TB and STI.
- 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. 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 (refer to annexure 9 for adult TB screening tool). Patients co-infected with TB are eligible for lifelong ART regardless of CD4 cell count.

Suspect TB if any of the following symptoms are present:

- Cough ≥2 weeks
- 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

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

- All TB patients with **CD4 <50**, as well as those with extra-pulmonary TB (**excluding** TB meningitis [TBM]) or any other WHO stage 4 infection, should be started on ART within **2 weeks** of initiation of TB treatment, when the patients symptoms are improving and TB treatment is tolerated.
- All TB patients with **CD4 >50** should start ART between **2 - 8 weeks** after initiation of TB treatment.
- Patients with **TBM or CM** should be started on ARVs within **4-6 weeks**.
- Efavirenz-based regimens are generally preferred to Nevirapine-based regimens in adolescents and adults with active TB on 1st line ART regimens.

Considerations of the timing in the 2-8 week period:

- Patients should be initiated on ART as soon as they are ready to start and tolerating their TB medication.
- The earlier a patient starts ART, the higher the chance of developing IRIS.
- 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 importance of keeping patients in care should be considered and patients should be offered adherence support at every visit.

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

- Continue ART throughout TB treatment.
- Adjust doses of Lopinavir/ritonavir if patient on Rifampicin-containing TB regimen (refer to table12)

Table 12: Management of Patients co-infected with TB requiring ART

TB diagnosed before starting ART	TB develops while on ART
CD4 <50 or stage 4: introduce ART within two weeks of starting TB treatment **CD4 >50:** introduce ART between 2- 8 weeks of starting TB treatment **Cryptococcal meningitis and TB meningitis:** start ART between 4- 6 weeks of starting TB treatment **Preferred first-line regimen (Late Adolescents & Adults):** Tenofovir + Emtricitabine + Efavirenz (provided as Fixed Dose Combination)	**Continue ARV therapy throughout TB treatment.** **Children & early adolescents:** **NNRTI- based regimen:** Patient can remain on their regimen **PI-based regimen:** Boost doses of Ritonavir for duration of TB treatment (refer to annexure 3). **Late adolescents & adults:** **NNRTI- based regimen** : Patient can remain on their regimen **PI-based regimen** : Adjust doses of Lopinavir/ritonavir. At weekly intervals, check ALT and increase from 2 tablets every 12 hours to 3 tablets every 12 hours for 1 week and then 4 tablets every 12 hours if ALT <50. 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.

- 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.

- Rifabutin must be **initiated** by an Infectious Disease specialist or experienced TB doctor.
- Doses may need to be adjusted-refer to table 13.
- 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.

Table 13: 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 **EVERY ALTERNATE** day OR **THREE times a WEEK** for 6 months of TB treatment

7. ISONIAZID PREVENTIVE THERAPY (IPT) FOR TREATMENT OF LATENT TB INFECTION IN HIV INFECTED PATIENTS

- All patients in HIV care must be screened for active TB at every clinic visit and started on ART if eligible.
- IPT is an effective intervention for preventing the development of active TB disease in clients with latent TB infection.

7.1 IPT in Children & Early Adolescents

- 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 IPT must repeat the course of therapy. This is not dependent on the interval between completion of treatment and re-exposure.
- Pre-exposure IPT is not recommended in HIV infected children.
- Children who have successfully completed TB treatment should not routinely receive IPT. 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
- Dosing: Isoniazid 10mg/kg/day (maximum 300mg every 24 hours) with
  Pyridoxine: <5 years - 12.5 mg every 24 hours
  >5 years - 25 mg every 24 hours
- Duration of IPT: 6 months

7.2 IPT in Late Adolescents & Adults

- All HIV infected late adolescents and adults should be assessed for IPT 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
- IPT is safe to use in pregnant or breastfeeding women.
- HIV- infected patients who were on drug-sensitive TB treatment previously may be started on IPT immediately after successful completion of a course of treatment.

How to Initiate and Manage IPT:

- If available, perform a Tuberculin Skin Test (TST).
- If the TST is positive, give IPT for a period of 36 months.
- If the TST is negative, give IPT for 12 months if the client is on ART. If not yet on ART, do not start IPT.
- If TST is not available, follow recommendations in table 14. TST should be done as soon as it becomes available.
- Dosing: Isoniazid 5mg/kg/day (maximum 300mg every 24 hours), with Pyridoxine 25mg every 24 hours.
- Screen clients on IPT for symptoms of active TB and side-effects of treatment at every clinic visit for duration of treatment.
- There is currently no evidence for repeating IPT in those who have completed 36 months or extending IPT beyond 36 months

Table 14: Summary of recommendations for IPT in late adolescents & adults

Summary Recommendations for IPT		
	Pre-ART (CD4 >500)	**On ART**
TST not available	IPT for 6 months**	IPT for 12 months
TST negative	No IPT	IPT for 12 months
TST positive	IPT for at least 36 months	IPT for at least 36 months
****note importance of doing TST within 6 months while on IPT. If TST positive, extend to 36 months. If TST negative, stop IPT.**		

8. COTRIMOXAZOLE PREVENTIVE THERAPY (CPT)

8.1 CPT in Children & Early Adolescents

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

- Indications for CPT:
  - HIV-exposed infants <I year - start at 4-6 weeks. Discontinue CPT once HIV infection is excluded by testing 6 weeks after final breastfeed
  - HIV-positive infants <1year regardless of CD4 count
  - HIV-positive children 1-5 years with WHO stage 2, 3 or 4; CD4 <25% or <500. Discontinue CPT if CD4 >500 on two consecutive occasions 3-6 months apart.
    If previous PCP: stop at 5 years old
  - HIV-positive children >5 years with WHO stage 3 or 4 or CD4 <200. Discontinue CPT if CD4 >200 on two consecutive occasions 3-6 months apart.
  - Co-infection with TB
- Contraindications: Known or suspected hypersensitivity to Sulphonamides/ Trimethoprim
- Recommended doses as per weight (see table15)
- 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 15: Paediatric 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	1 tablet

8.2 CPT in Late Adolescents & Adults on ART

- Indications for CPT :
  - CD4 <200
  - Co-infection with TB
  - Any WHO stage 3 or 4 condition
- CPT is safe to use in pregnancy and breastfeeding.
- Recommended dose of CPT: Cotrimoxazole 160/800mg every 24 hours.
- Contraindications and side effects as per children (see above)
- Alternative to CPT: Dapsone 100mg every 24 hours for clients with mild hypersensitivity to Cotrimoxazole. Do not use Dapsone if reaction was severe.

9. CRYPTOCOCCAL SCREENING AND TREATMENT

9.1 Cryptococcal Prophylactic Treatment in Children & Early Adolescents

- Cryptococcal screening is not performed routinely in children and early adolescents
- Those who are diagnosed and treated for Crytococcal 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/mm³ on at least two occasions.

9.2 Cryptococcal Screening and Treatment in Late Adolescents & Adults

- Cryptococcal menigitis (CM) is a serious opportunistic infection that can affect HIV-positive people with CD4 counts <100.
- A cryptococcal antigen test (CrAg or CLAT) should be performed on all late adolescents and adults with CD4 <100 before initiation of ART.
- Patients with previous diagnosis of CM do not need to be screened.
- Review result within a week.
- Management of patients with CrAg/CLAT positive result (see figure 3):

  - 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 intravenous Amphotericin B and oral Fluconazole 800mg daily in hospital for 2 weeks, followed by Fluconazole 400mg daily for 2 months, then 200mg daily.

    Delay **ART initiation by 4-6 weeks**.

  - If asymptomatic for CM or symptomatic patients with LP not suggestive of CM-

    Give oral Fluconazole 800mg daily for 2 weeks, followed by Fluconazole 400mg daily for 2 months, then 200mg daily. ART may be started **2 weeks** after initiation of Fluconazole prophylaxis.

- Duration of treatment:
  - Continue Fluconazole for minimum of 1 year in total and discontinue when the patient has two CD4 counts >200 taken at least 6 months apart
- Precautions:
  - Pregnant women with CrAg/CLAT positive **must** be discussed with a specialist before Fluconazole is prescribed.
  - 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**.

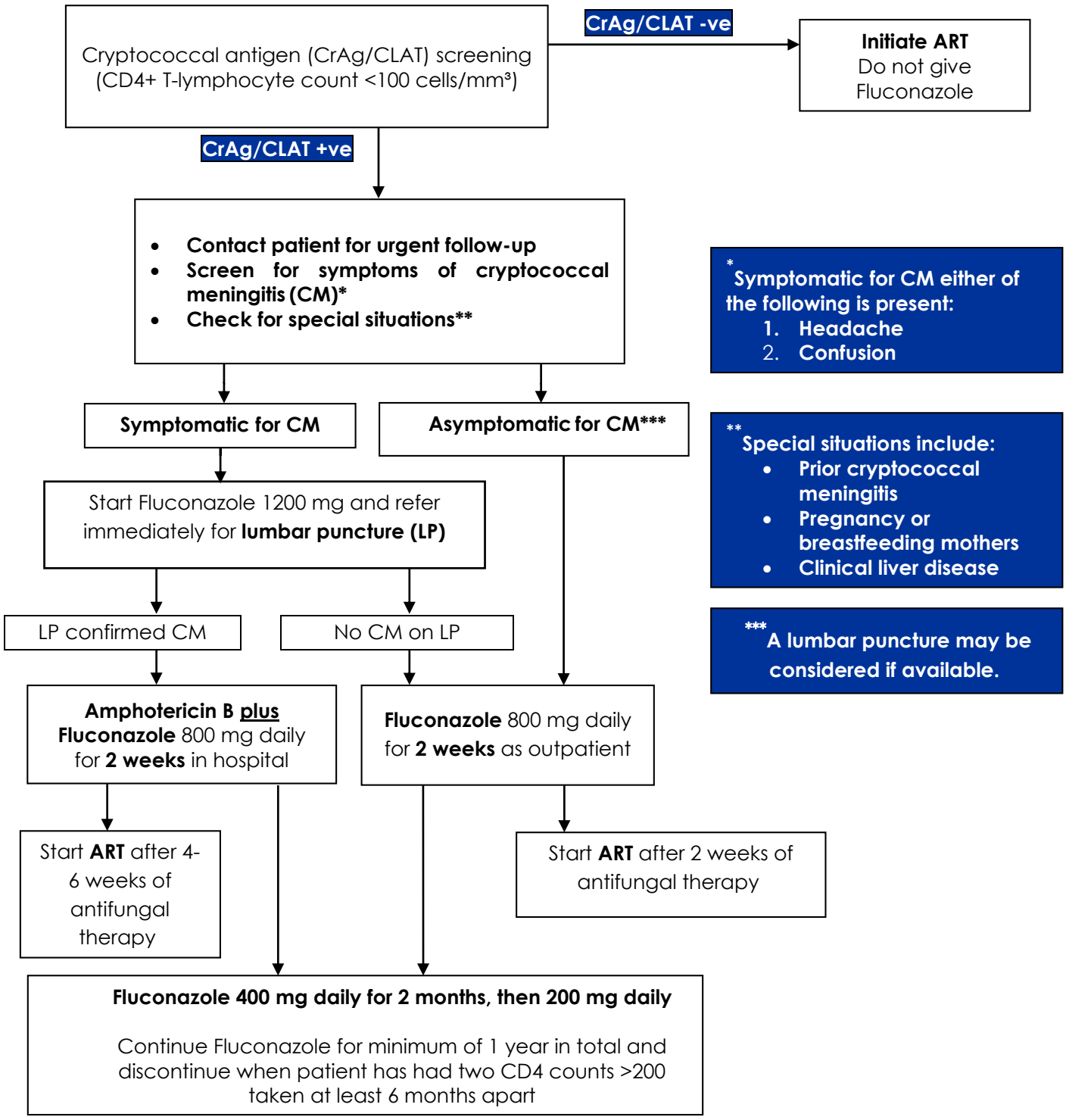


Figure 3: Simplified Algorithm for Cryptococcal screening and treatment in late adolescents and adults

10. 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?

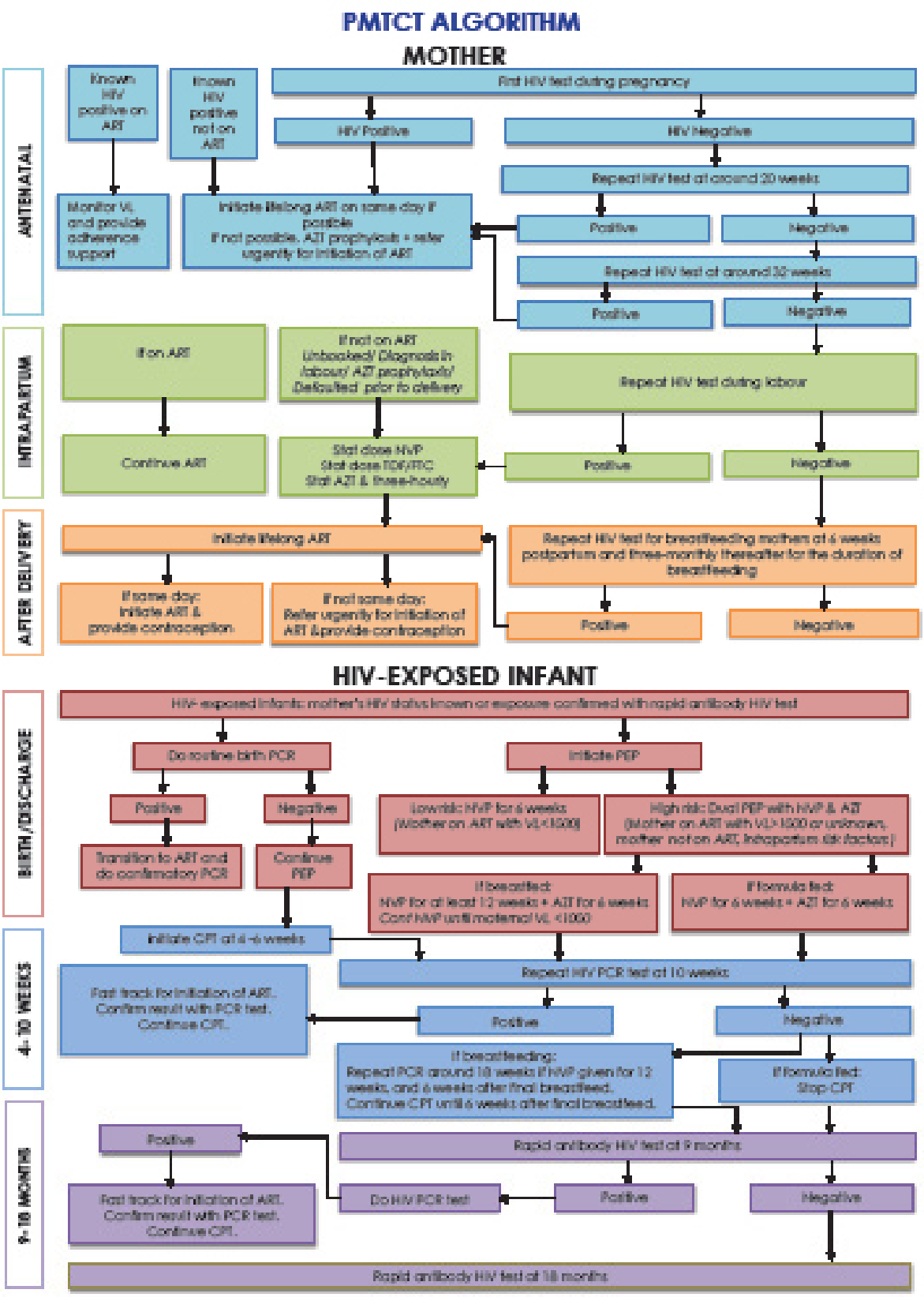
- Report the following ADR's:
    - All ADR's to newly marketed drugs or new drugs added to the EDL
    - All serious reactions and interactions
    - ADR's that are not clearly stated in the package insert
    - All adverse reactions or poisonings to traditional or herbal remedies

- Report even if you are not certain that the medicine caused the event

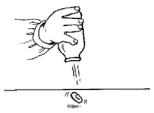
- Report suspected product quality problems :
    - Suspected contamination
    - Questionable stability
    - Defective components
    - Poor packaging or labelling
    - Therapeutic failures

- How to report an ADR:
  Fill in an adverse drug reaction/ product quality report form (refer to annexure 10) and submit to pharmacist.

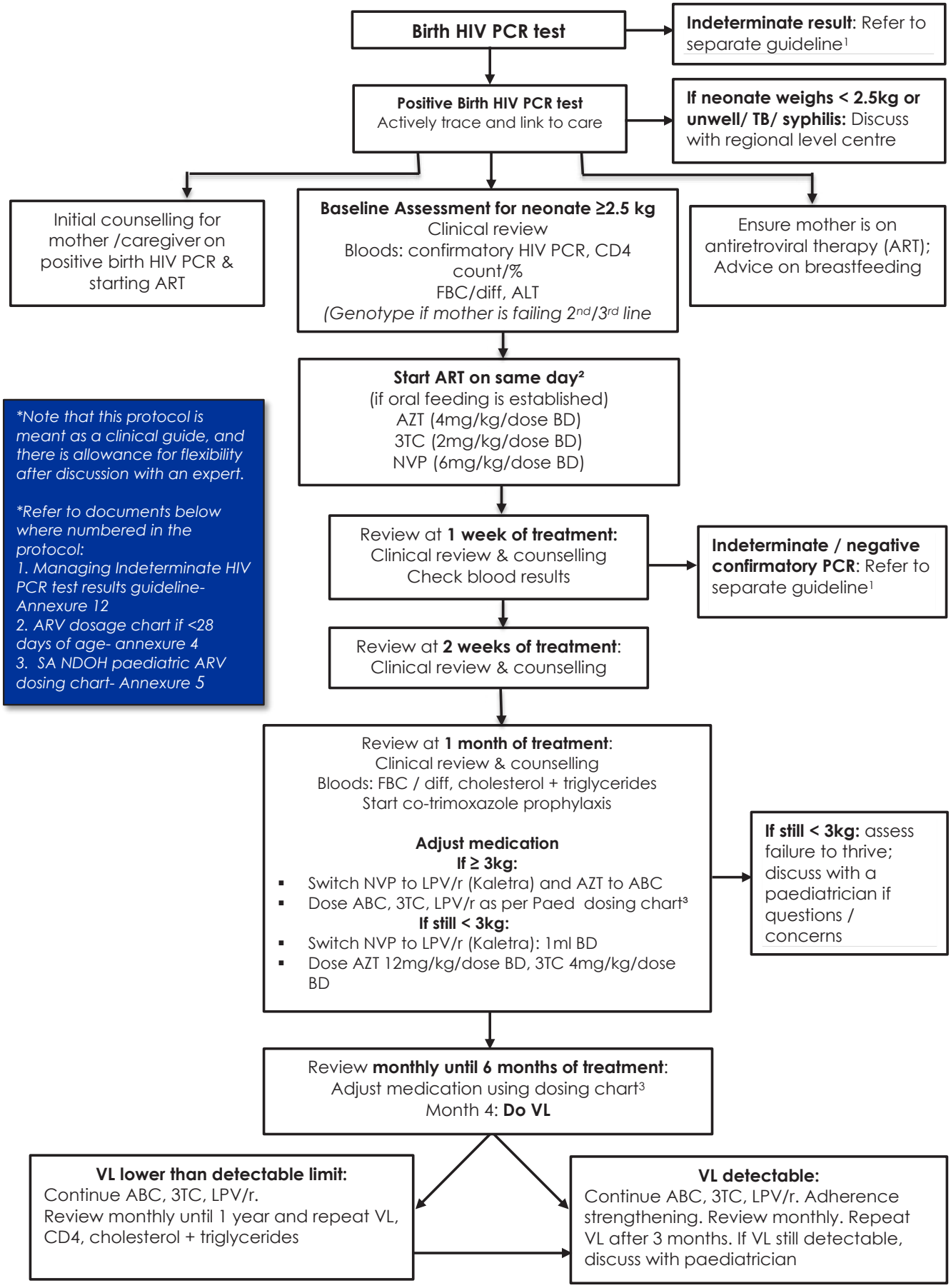
Annexure 1: PMTCT Algorithm



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 ≥2.5 kg at birth

	Lamivudine (3TC)		Zidovudine (AZT)		Nevirapine (NVP)	
Target dose	2mg/kg/dose TWICE daily (BD)		4mg/kg/dose TWICE daily (BD)		6mg/kg/dose TWICE daily (BD)	
Available formulation	10mg/ml		10mg/ml		10mg/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	0.6 ml BD	6 mg BD	1.2 ml BD	12 mg BD	1.8 ml BD	18 mg BD
≥3.0-<3.5	0.7 ml BD	7 mg BD	1.4 ml BD	14 mg BD	2.1 ml BD	21 mg BD
≥3.5-<4.0	0.8 ml BD	8 mg BD	1.6 ml BD	16 mg BD	2.4 ml BD	24 mg BD
≥4.0-<4.5	0.9 ml BD	9 mg BD	1.8 ml BD	18 mg BD	2.7 ml BD	27 mg BD
≥4.5-<5.5	1.0 ml BD	10 mg BD	2.0 ml BD	20 mg BD	3.0 ml BD	30 mg BD
≥5.5-<6.5	1.2ml BD	12 mg BD	2.4 ml BD	24 mg BD	3.6 ml BD	36 mg BD

Caregivers who will be administering ARV medication to the child must be supplied with a syringe (1ml or 2ml) for each of the 3 ARVs and shown how to prepare and administer the correct dose. If possible, 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.

Annexure 5: Dosing of 1st and 2nd line ARVs in Children & Early Adolescents

Western Cape Government Health
BETTER TOGETHER.

ANTIRETROVIRAL DRUG DOSING CHART FOR CHILDREN 2013

health Department Health REPUBLIC OF SOUTH AFRICA

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

	Abacavir (ABC)		Lamivudine (3TC)		Efavirenz (EFV)	Lopinavir/ritonavir (LPV/rtv)	Ritonavir boosting (RTV)	Stavudine (d4T)	Didanosine (ddI)	Nevirapine (NVP)	Zidovudine (AZT)	
Target Dose	8mg/kg TWICE daily **OR** **≥10kg:** 16mg/kg ONCE daily		4mg/kg TWICE daily **OR** **≥10kg:** 8mg/kg ONCE daily		By weight band **ONCE** daily	300/75mg/m²/dose LPV/rtv **TWICE** daily	ONLY as booster for LPV/rtv when on Rifampicin **TWICE** daily (0.75xLPV dose bd)	1mg/kg/dose **TWICE** daily	180-240mg/m²/dose **ONCE** daily	160-200 mg/m²/dose **TWICE** daily (after once daily lead-in x 2 wks)	180-240mg/m²/dose **TWICE** daily	**Target Dose**
Available Formulations	Sol 20mg/ml Tabs 60mg (scored dispersible), 300mg (not scored), ABC/3TC 600/300mg		Sol. 10mg/ml Tabs 150mg (scored), 300mg, ABC/3TC 600/300mg		Caps 50,200mg Tabs 50,200, 600mg (not scored)	Sol. 80/20mg/ml Adult Tabs 200/50mg, Paeds Tabs 100/25mg	Sol. 80mg/ml	Sol. 1mg/ml Caps 15,20,30mg	Tabs 25,50,100mg (dispersible in 30ml water) Caps 250mg EC	Sol. 10mg/ml Tabs 200mg (scored)	Sol. 10mg/ml Caps 100mg Tabs 300mg (not scored), AZT/3TC 300/150mg	**Available Formulations**
Wt. (kg)	**Currently available tablet formulations of abacavir (except 60mg), efavirenz, LPV/rtv and AZT must be swallowed whole and NOT chewed, divided or crushed**											**Wt. (kg)**
<3	**Consult with a clinician experienced in paediatric ARV prescribing for neonates (<28 days of age) and infants weighing <3kg**											**<3**
3-3.9	2ml bd		2ml bd		**Avoid using when <10kg or <3 years:** dosing not established	*1ml bd	1ml bd	6ml	Avoid	5ml bd	6ml bd	**3-3.9**
4-4.9												**4-4.9**
5-5.9	3ml bd		3ml bd			*1.5ml bd	1.5ml bd	**7.5mg bd:** open 15mg capsule into 5ml water: give 2.5ml	100mg od: *(2x50mg tabs)*			**5-5.9**
6-6.9									125mg od: *(1x100mg + 1x25mg tabs)*	8ml bd	9ml bd	**6-6.9**
7-7.9	4ml bd		4ml bd					**10mg bd:** open 20mg capsule into 5ml water: give 2.5ml				**7-7.9**
8-8.9											1 cap bd OR 12ml bd	**8-8.9**
9-9.9												**9-9.9**
10-10.9	Choose only one option: 6ml bd OR 2x60mg tabs bd	12ml od OR 4x60mg tabs od	Choose only one option: 6ml bd	12ml od	200mg nocte *(1x200mg cap/tab)*	2ml bd	1.5ml bd	**15mg bd:** open 15mg capsule into 5ml water	150mg od: *(1x100mg + 1x50mg tabs)*	10ml bd		**10-10.9**
11-13.9												**11-13.9**
14-16.9	8ml bd OR 2.5x60mg tabs bd	5x60mg tabs od OR 1x300mg tab od OR 15ml od	½ x150mg tab bd OR 8ml bd	1x150mg tab od OR 15ml od	300mg nocte: *(200mg cap/tab + 2x50mg cap/tab)*	Choose one option: -2.5ml bd -100/25mg **paeds tabs:** 2 bd -200/50mg **adult tabs:** 1 bd	2ml bd	**20mg bd:** open 20mg capsule into 5ml water (if the child is unable to swallow a capsule)	175mg od: *(1x100mg + 1x50mg + 1x25mg)*	1 tab am ½ tab pm OR 15ml bd	2 caps am 1 cap pm OR 15ml bd	**14-16.9**
17-19.9												**17-19.9**
20-22.9	10ml bd OR 3x60mg tabs bd	1x300mg tab + 1x60mg tab od	1x150mg tab bd OR 15ml bd	2x150mg tab od OR 1x300mg tab od OR 30ml od		Choose one option: -3ml bd - 100/25mg **paeds tabs:** 2 bd - 200/50mg **adult tabs:** 1 bd	2.5ml bd		200mg od: *(2x100mg tabs)*		2 caps bd OR 20ml bd	**20-22.9**
23-24.9		1x300mg tab + 2x60mg tabs od										**23-24.9**
25-29.9	1x300mg tab bd	2x300mg tabs od OR 1xABC/3TC 600/300mg tab od	1x150mg tab bd	2x150mg tabs od OR 1x300mg tab od OR 1xABC/3TC 600/300mg tab od	400mg nocte: *(2x200mg caps/tabs)*	Choose one option: - 3.5ml bd - 100/25mg **paeds tabs:** 3 bd - #200/50mg **adult tabs:** 1 bd + 100/25mg **paeds tabs:** 1 bd	3ml bd	**30mg bd**	250mg od: *(2x100mg + 1x50mg tab)* OR 1x250mg EC cap od	1 tab bd	1x300mg tab bd OR 1xAZT/3TC 300/150mg tab bd	**25-29.9**
30-34.9						Choose one option: - 4ml bd - 100/25mg **paeds tabs:** 3 bd - #200/50mg **adult tabs:** 1 bd + 100/25mg **paeds tabs:** 1 bd						**30-34.9**
35-39.9						Choose one option: - 5ml bd - 200/50mg **adult tabs:** 2 bd	4ml bd					**35-39.9**
>40					600mg tab nocte							**>40**

od = once a day
(usually at night)
bd = twice a day

* Avoid LPV/rtv solution in any full term infant <14 days of age and any premature infant <14 days after their due date of delivery (40 weeks post conception) or obtain expert advice.
# Children 25-34.9kg may also be dosed with LPV/rtv 200/50mg adult tabs: 2 tabs am; 1 tab pm

Weight (kg)	**3-4.9**	**5-9.9**	**10-13.9**	**14-29.9**	**≥30**
Cotrimoxazole Dose	2.5ml od	5ml od	5ml od	10ml or 1 tab od	2 tabs od
Multivitamin Dose	2.5ml od	2.5ml od	5ml od	5ml od	10ml or 1 tab od

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

1. Darunavir (DRV) and Ritonavir (RTV)

- Formulations available:
  - Tablets: 75 mg, 150mg, 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 200mg (2.0 ml) + RTV 32 mg (0.4 ml)	Should only be used of patient is resistant to Lopinavir Children <3 years of age OR <10kg: DRV is not recommended
11 - <12	DRV 220mg (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 375 mg (combination of 2 x 150 mg + 1 x 75 mg tablets or 3.8 ml) + RTV 48 mg (0.6 ml)	
30 - <40	DRV 450 mg (combination of 3 x 150 mg tablets or 4.6 ml) + RTV 100 mg capsule (or 1.25 ml)	
≥40	DRV 600 mg (1 x 600 mg tablet or 6 ml) + RTV 100 mg capsule (or 1.25 ml)	

- Adolescent (aged ≥18 years of age)/ adult dose (treatment experienced with ≥1 DRV resistance-associated mutation):
  DRV 600 mg + RTV 100 mg both twice daily with food

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
  - For oral suspension: single use packet of 100 mg (Not yet registered in SA, available on compassionate use access from manufacturer with MCC Sec 21 aproval)

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	1 ml (20mg) 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	1.5 ml (30 mg) twice daily	
6 - <8	2 ml (40 mg) twice daily	
8 - <11	3 ml (60 mg) twice daily	
11 - <14	4 ml (80 mg) twice daily	
14 - <20	5 ml (100 mg) twice daily	

Children ≥2 - <6 years of age: dosing of chewable tablets:

Weight band (kg)	Dose of Raltegravir	Number of chewable tablets
7 - <10	50 mg twice daily	0.5 x 100 mg twice daily
10 - <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

- Children ≥2 - <12 years of age:
  Two dosing options:
  1. If < 25 kg body weight, chewable tablets by weight-based dosing chart above to maximum of 300 mg twice daily
  2. If ≥ 25 kg body weight, 400 mg film-coated tablet twice daily
- Adolescent (aged ≥12 years of age) / adult dose:
  400 mg film-coated tablet twice daily

3. Etravirine (ETR)

- Formulations available:
  Tablets: 25 mg (Not yet registered in SA, available on compassionate use access from manufacturer with MCC Sec 21 approval)
  100 mg (registered with MCC)

- Children <6 years of age: not recommended

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	

Annexure 7: Dosing of ARVs in Late Adolescents & Adults

ARV Dosing Guide for Late Adolescents & Adults		
Drug	**Standard Dose**	**Side-effects**
Nucleoside & Nucleotide Reverse Transcriptase Inhibitors (NRTI's)		
Abacavir (ABC)	300mg 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 daily (If <40kg, 400mg at night daily)	Rash, hepatitis, CNS effects, gynaecomastia
Etravirine (ETR)	200mg 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 (ATZ)	300mg daily plus Ritonavir 100mg with food	Jaundice (due to unconjugated hyperbilirubinaemia), dyslipidaemia
Darunavir (DRV)	600mg twice daily plus Ritonavir 100mg with food	Diarrhoea, nausea, rash, dyslipidaemia (low potential)
Integrase Strand Transfer Inhibitors (InSTI's)		
Raltegravir (RAL)	400mg twice daily	Rash (including Stevens-Johnson), hepatitis, nausea, diarrhoea

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
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	

Simplified modified Cockcroft and Gault formula to calculate Creatinine Clearance (CrCl) in Adults/Adolescents >16years:

$$\text{CrCl [ml/min]} = \frac{(140 - \text{age}) \times \text{Wt (kg)}}{\text{Serum Cr } (\mu\text{ml/L})}$$

For women: multiply by 0.85

Annexure 9: 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/m^2)		**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 discontinuation	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?
Was 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 m^2)		
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: _____ Date: _____

Clinician's name: _____

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 10: TB Suspect Screening Tool

Revised 15 April 2013 Ref: CT/TB 5/05

TB SUSPECT SCREENING TOOL

For TB-suspects, contacts, prophylaxis in HIV. To be used as part of PALSA Plus based screening.

History (This section can be completed by administrative support staff)

PATIENT PERSONAL DETAILS (add patient sticker)	Name	Folder number
	Surname	Clinic
	Address	Date of Birth
		Contact No

TB HISTORY	Previous TB	Y	N	Year		Clinic	
	Previous treatment outcome	Cure		Complete	Default	Failure	Transfer
	Previous MDR-TB	Y	N	Outcome	Default	Failure	Cure

HISTORY OF CONTACT	Known contact with confirmed TB patient			Y	N		
	MDR/XDR contact	Y	N	Name		Clinic	
	MDR/XDR contact resistance pattern						

EXPOSURE RISK	Health worker	Y	N	Mines / Quarry / Sandblasting…	Y	N
	Prisoner	Y	N	Other	Y	N

TB SYMPTOMS	**Adults**			**Children < 8 years**		
	Cough > 2 weeks	Y	N	Cough/wheeze > 2 weeks	Y	N
	Drenching night sweats	Y	N	Fatigue (child does not play)	Y	N
	Blood stained sputum	Y	N	Fever ≥ 2 weeks	Y	N
	Weight loss	Y	N	Weight loss	Y	N
	Fever ≥ 2 weeks	Y	N	Not gaining weight (failure to thrive)	Y	N
	Chest pain on breathing	Y	N			

Action (This section to be completed by Clinician (PN/EN and /or MO)

HCT	HIV	Pos	Neg	Refused	CD4 result	
	ART	Y	N	ARV Start Date		

OBSERVATIONS	Weight		kg	Failure to thrive (check growth curve in RTH Card)	Y	N
	Temperature		C	Neck stiffness	Y	N
	Respiratory rate		/min	Visiable masses neck/axilla/groin	Y	N
	BP		mmHg			
	Pulse		/min			

TB SKIN TEST	Mantoux	Date		Date read		Result	

SPUTUM BACTERIOLOGY	Specimen	Test	Date	Lab no	Result	DST	
						Rif (S/R)	INH (S/R)
	1.						
	2.						
	3.						
	4.						
	5.						

ANTIBIOTIC	Name antibiotic	Y	N	Date	

NURSE-BASED DIAGNOSIS AND ACTION	Adult **NO TB**: Prophylaxis **not** required		Unconfirmed TB & still symptomatic: **Refer** to Medical Officer	
	Child < 5 years and/or HIV +ve **NO TB**: Prophylaxis required		Confirmed TB (Notify & treat for TB	
			Confirmed DR-TB refer to Medical Officer	

NAME & SIGNATURE (PN/MO)		Date		Follow up	Date	
					Date	

Annexure 11: WC Adverse Drug Reaction Reporting Form

Western Cape Adverse Drug Reaction Reporting Form for patients on ARV & / or TB treatment

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

MEDICATION HISTORY (circle suspected medicines)

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

ADVERSE REACTION DETAILS

- ☐ **Anaemia requiring transfusion** — ***Hb:***
- ☐ **Cholestatic hepatitis**
- ☐ **Congenital anomaly/ Pregnancy exposure/ foetal death**
- ☐ **Gynaecomastia**
- ☐ **Hypersensitivity reaction**
- ☐ **Hyperuricaemia**
- ☐ **Lactic acidosis** *(Metabolic acidosis and lactate>2mmol/L)*
- ☐ **Lipoatrophy** *(Fat loss)*
- ☐ **Lipohypertrophy** *(Abnormal fat accumulation)*
- ☐ **Neutropenia** *(Neutrophils less than 0.5 X 10⁹/L)*
- ☐ **Other** — **Describe:**
- ☐ **Ototoxicity**
- ☐ **Pancreatitis**
- ☐ **Renal toxicity** — ***Creatinine (µmol/L):***
- ☐ **Skin reaction**
- ☐ **SJS/TEN**
- ☐ **Symptomatic hyperlactataemia** ***(lactate>2 and symptoms)***
- ☐ **Transaminitis** *(gr 3=5-10XULN, gr 4>10XULN)/* **symp hepatitis**
- ☐ **Death**

Suspected cause of death:

Description of reaction:

Date event started:

Investigations (including other relevant medical history):

Management of adverse event:

OUTCOME

	Died	Recovered	Not yet recovered	Permanent damage/ disability	Hospita-lised	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 12: SOP for Mangement of Indeterminate HIV-PCR Results Aug 2015

STANDARD OPERATING PROCEDURE

Title:	**Managing INDETERMINATE HIV PCR Test Results**
Document number:	001
Version number:	001

Written by:	Prof. Gayle Sherman, Dr Ahmad Haeri Mazanderani
Reviewed by:	Dr Sergio Carmona, Dr Marvin Hsiao, Dr Karl Technau, Dr Leon Levin, Prof Mark Cotton, Prof Brian Eley, Dr Max Kroon, Prof Ute Feucht, Dr Lee Fairlie, Dr Catherine Wedderburn, Dr Ute Hallbauer, Dr David Moore, Prof Landon Myer, Prof Theunis Avenant, Dr Nicolette du Plessis and Members of the NHLS Virology Expert Committee
Active from:	1 August 2015

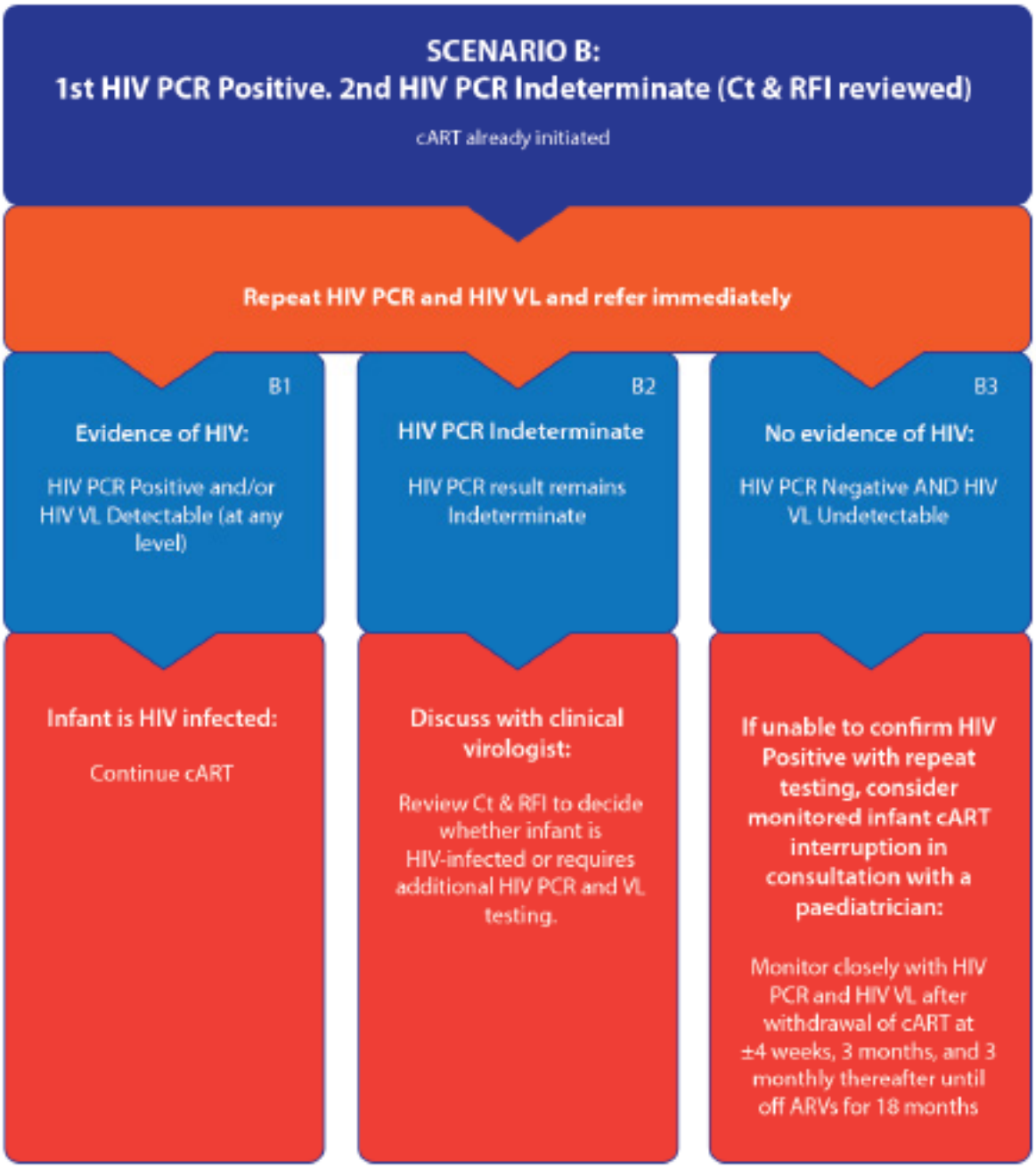
Table of Content

Summary

- The laboratory diagnosis of HIV in infants <18 months of age requires two HIV PCR positive results, each on a separate specimen, as per National HIV Paediatric testing guidelines of 1 June 2015 (alternatively, one HIV PCR positive result in association with an HIV viral load that is detectable on a separate specimen is also diagnostic of HIV)
- An HIV PCR result can be positive, negative or indeterminate
- An indeterminate HIV PCR result means that the test is inconclusive (i.e. it is not clearly positive or negative) and requires immediate FURTHER TESTING to determine whether the infant is HIV infected or not and REFERRAL.
- Repeat HIV PCR and HIV viral load testing needs to be performed as a matter of urgency and the patient managed accordingly (see Flow Diagram Scenario A for managing initial HIV PCR indeterminate cases and Flow Diagram Scenario B for managing confirmatory HIV PCR indeterminate cases)
- Infants in which the diagnosis of HIV remains inconclusive or where discordant results have been obtained (i.e. a positive HIV PCR followed by a negative HIV PCR and undetectable HIV viral load) need to be managed by a multidisciplinary team and should be discussed as a matter of urgency with a specialist clinician and pathologist (see contact details below). Repeat HIV testing and clinical monitoring is required until an HIV status is established
- It is important to remember that infants cannot be considered HIV-uninfected unless repeat testing occurs at least 4 weeks after infant prophylaxis (or cART has been discontinued), and six weeks after cessation of breastfeeding
- Counseling the mother/primary caregiver regarding the indeterminate result is of paramount importance to ensure successful follow-up and arriving at a definitive diagnosis (see COUNSELING box below)

Flow Diagram A:

Flow Diagram B:



Introduction

According to the National HIV Paediatric testing guidelines of 1 June 2015, all HIV-exposed infants should be tested for HIV infection, using a molecular based assay such as PCR (polymerase chain reaction), at birth, 10 weeks of age and 6 weeks after stopping breastfeeding if still under 18 months of age at that time.[1] In children receiving prolonged nevirapine prophylaxis to 12 weeks of age, an additional HIV PCR test is required at 18 weeks (or 14 weeks of age in some provinces).
The most common specimen collected from an infant is capillary whole blood from a heel prick spotted onto a cotton based paper card, which is dried at the site of collection. This is known as a dried blood spot (DBS) and requires three full spots per card. EDTA (purple top tube) anti-coagulated whole blood is also suitable and can replace a DBS; the minimum volume is 250µl (0.25mL).

The HIV PCR results should generally be available within THREE working days of reaching the nearest NHLS PCR laboratory.

Reporting of an HIV PCR result has 4 options:

1) **POSITIVE**, meaning that HIV is detected in the sample,

2) **NEGATIVE**, meaning that HIV is not detected in the sample,

3) **INDETERMINATE** result or

4) **OTHER** results *e.g.* 'insufficient sample'; 'clerical error'; 'invalid result', etc. These infants require submission of a repeat sample for HIV PCR as soon as possible.

Purpose

This SOP provides guidance for NHLS laboratory staff and the relevant clinical care providers on managing INDETERMINATE HIV PCR results.

Definitions:

ART:	Antiretroviral therapy
cART:	Combination antiretroviral therapy
Ct:	Cycle threshold
NDoH:	National Department of Health
DBS:	Dried Blood Spot
DCST:	District Clinical Specialist Team paediatrician or paediatric nurse
EDTA tube:	Blood collection tube with a purple top to prevent coagulation
EID:	Early Infant Diagnosis
HAST:	HIV AIDS STD

HIV:	Human Immunodeficiency Virus
NHLS:	National Health Laboratory Service
Lab:	EID NHLS laboratory
LIS:	Laboratory Information System
MCDS:	Minimal Clinical Data Set
NVP:	Nevirapine
PCR:	Polymerase chain reaction
PMTCT:	Prevention of mother-to-child transmission
RFI:	Relative fluorescence intensity
RTHB:	Road to Health Booklet
SOP:	Standard Operating Procedure
TAT:	Turnaround time
VL:	Viral load

Responsibilities

Clinical care givers

1. Identify HIV-exposed neonates or infants
2. Counsel the care provider and obtain consent for testing
3. Collect the blood specimen as required
4. Complete the NHLS request form with complete minimal clinical data set (MCDS) to ensure results can be returned accurately to the correct clinician in time and that there is a record of the parent's/caregiver's physical address and telephone contact numbers to link infants to care. Ensure the NHLS requisition barcode sticker is placed into the infant's RTHB for ease of tracing the PCR result.
5. For a follow-up specimen, please specify all previous HIV PCR and HIV VL results on the request form with either the laboratory barcode or episode number.

Pathologist and lab staff

1. Provide HIV PCR results within the agreed TAT
2. Review results according to the corresponding SOP and authorize results
3. Prioritize indeterminate HIV PCR results since these infants may be HIV infected and run the risk of increased morbidity and mortality due to delayed cART initiation or unnecessary cART in an uninfected infant
4. Ensure there is a record-keeping system for all indeterminate HIV PCR results
5. Ensure there is a notification system for the relevant clinical staff for all indeterminate HIV PCR results

Procedures:

What does an indeterminate HIV PCR test result mean?
An indeterminate result means that

- The HIV PCR test is inconclusive *i.e.* it is not clearly positive or negative
- Either HIV is present at very low levels that can only just be detected or HIV is absent.

Either way, **urgent repeat** HIV testing is essential to establish the child's HIV status. Such children may either be HIV-infected or uninfected on additional testing. Repeat blood samples should preferably be EDTA (purple top) anti-coagulated whole blood for HIV PCR **AND** HIV VL. If this is not possible, submit DBS for repeat HIV PCR testing and refer immediately for EDTA whole blood sampling for HIV VL testing.

Indeterminate results occur infrequently (in less than 1% of all HIV PCR tests) but are problematic to manage. Uncertainty of the infant's HIV infection status can result in poor outcomes *e.g.* lifelong treatment in HIV-uninfected infants, or morbidity and mortality due to delayed treatment in HIV-infected infants.

An **HIV-infected child** has at least TWO positive HIV virological assays (either an HIV PCR or HIV VL) on TWO separate samples.

An **HIV-uninfected child** has a negative HIV virological assay on a sample taken ±4 weeks after all infant ARV prophylaxis has been discontinued provided that no breastfeeding has occurred in the last 6 weeks. These children require follow up testing as per the national guidelines.

Responding to indeterminate results requires a multidisciplinary approach from clinicians and pathologists. Depending on the referral structures in each district, the primary clinician should urgently seek advice for each case from more specialized clinicians (*e.g.* DCST paediatricians, paediatric infectious disease specialists) and pathologists based at the NHLS HIV PCR laboratories as well as PMTCT/HAST program managers.

Every primary clinician should have contact details of specialist clinicians, program managers and their NHLS virology laboratory from the outset. Accurate completion of the NHLS requisition form with patient and clinician contact details facilitates this multidisciplinary approach and should include at least the following: clinic/hospital name, name and surname of patient, date of birth, sex, file number, patient address and contact details, specimen type and collection date, and the health care workers name, registration number and contact details [refer to the Minimal Clinical Data Set – MCDS SOP]. Please take special care to ensure that the details on the request form reflect those on the specimen (*i.e.* ensure that the name, surname and barcode on the form and on the specimen are the same).

Figure1: Example of an NHLS request form

PLEASE TEAR HERE PLEASE TEAR HERE PLEASE TEAR HERE PLEASE TEAR HERE PLEASE TEAR HERE

NATIONAL HEALTH LABORATORY SERVICE

Practice number 5200296

PRIMARY HEALTH CARE

MARK IF URGENT ☐

NHLS LAB NUMBER BARCODE

AAAA0001P

LOC	
CHC / CLINIC / HOSP	
WARD	
WSR APPROV. CODE	
COPY REPORT TO	

SPEC			
SPECIMEN			
ANATOMICAL SITE			
COLLECTION DATE		TIME	
COLLECTED BY			

PATIENT			
PATIENT ID NO		ID / Passport	
HOSPITAL NUMBER			
SURNAME			
FIRST NAME		SEX	M F
DATE OF BIRTH	D D / M M / Y Y Y Y	AGE	
RACE		TITLE	
PATIENT ADDRESS			
PATIENT TEL NO	H	W	C

CLIN			
CLINICAL INFORMATION		ICD10 DIAGNOSIS CODES	
MEDICATION		Warfarin	Heparin

HCW	
CLINICIAN / HCW NAME	
HPCSA / SANC NO	
PRACTICE NO	
CONTACT NO	
EMAIL ADDRESS	
CLINICIAN'S SIGNATURE	

PRIVATE ACCOUNT			
AUTHORISATION NO		FEE CLASS	
MEDICAL AID		PLAN	
MEDICAL AID NO		DEP CODE	
MEMBER NAME			
MEMBER ID NO			
MEMBER ADDRESS			
MEMBER TEL NO			
EMPLOYER			
MEMBER'S SIGNATURE	I consent to tests and take responsibility for payment of this account		

Actions

The actions required by Clinical Staff:

The actions required following an indeterminate result are described in two broad scenarios **A** and **B** (see flow diagram above)

Scenario A: The first HIV PCR test has an **indeterminate** result:

Action: ***Repeat*** an HIV PCR **AND** HIV VL test immediately and *refer* (as per national guidelines page 27). Do not await the repeat HIV PCR and VL results before referring (see 'Referrals' section below).

A1: The repeat HIV PCR is positive and/or HIV VL is detectable (*i.e.* any value above the detection limit of the assay): the child is likely HIV infected. Infant cART initiation should not be delayed by further testing. Although these cases require a confirmatory HIV PCR and/or VL to definitively establish a positive HIV infection status, the clinical team must consider each case individually. In some cases an indeterminate HIV PCR result (depending on Ct/RFI values) followed by a positive HIV PCR and/or detectable HIV VL result may be enough to establish a diagnosis of HIV infection. If not, confirmatory HIV PCR and HIV VL tests are required.

Action: cART initiation following submission of specimen for confirmatory HIV PCR and HIV VL if necessary.

A2: The repeat HIV PCR is negative or indeterminate again **AND** the HIV VL is undetectable: HIV infection cannot be excluded in the presence of antiretroviral prophylaxis (*e.g.* daily NVP) or within 4 weeks of discontinuing prophylaxis.

Action: Complete the infant ART prophylaxis course (*i.e.* infant NVP syrup, usually for 6 weeks) and repeat HIV PCR **AND** HIV VL 4 weeks later. Monitor the child clinically every 2 weeks. If the child becomes symptomatic for HIV infection, repeat testing immediately. Healthcare workers should have a low threshold for repeat HIV PCR testing at any opportunity before 10-18 weeks.

Scenario B: The first HIV PCR is positive but the second, confirmatory HIV PCR is indeterminate:

Action: Repeat the HIV PCR **AND** HIV VL test immediately and refer. Do not await the repeat HIV PCR and VL results before referring (see 'Referrals' section below).

B1: The repeat HIV PCR is positive and/or HIV VL is detectable (*i.e.* any value above the detection limit of the assay): the child is confirmed HIV-infected because HIV would have been detected twice on separate samples.

Action: Continue cART.

B2: The repeat HIV PCR is indeterminate and HIV VL is undetectable.

Action: Review the Ct and RFI in consultation with a clinical virologist to decide whether the infant can be considered HIV-infected or whether HIV PCR and HIV VL require repeating.

B3: The repeat HIV PCR is negative **AND** the HIV VL undetectable: HIV infection cannot be excluded in the presence of antiretroviral prophylaxis (daily NVP) or cART if already initiated.

Action: The best approach for these infants should be determined within the multidisciplinary team. It is vital to keep the patient's caregiver informed and supported (see 'Counselling Suggestions' below) and the patient kept in close clinical follow up. The same approach should be followed for infants with repeatedly indeterminate HIV PCR results.

In all cases, a clear plan should be documented, communicated and adhered to. If the diagnosis remains unclear despite all attempts to resolve, the last resort is a monitored treatment interruption, if treatment has been started, with follow-up testing at one month, three months, and three monthly thereafter for a minimum of 18 months off ART.

The actions required by Pathologist and Laboratory staff

HIV VIROLOGY LABORATORIES

Indeterminate results, currently defined as Ct >33 and/or RFI <5, should be treated as urgent and only authorized after careful review by a virology registrar or consultant. The Ct & RFI values should be documented on the LIS. Consider:

- TRAK search to identify previous HIV PCR and HIV VL test result(s)
- Contact clinician who sent the HIV PCR test and/or designated centralized responsible person for district or province (*e.g.* paediatric infectious disease specialist/PMTCT coordinator/DCST paediatrician) to discuss case and request repeat samples as soon as possible
- Repeat HIV PCR test **AND** HIV VL (if possible on DBS) on the 'indeterminate' sample after alerting the field i.e. don't delay result in laboratory
- Where clinicians cannot be reached, kindly refer these cases and all available information to Drs Gayle Sherman (gayles@nicd.ac.za) or Ahmad Haeri Mazanderani (ahmadh@nicd.ac.za).

References:

1. South African National Department of Health. National Consolidated Guidelines for the Prevention of Mother-to-Child Transmission of HIV (PMTCT) and the Management of HIV in Children, Adolescents and Adults. Pretoria: Department of Health, 2015.

REFERRALS:

Referrals can mean seeking advice from clinicians and/or virologists or sending the patient to a specialist referral center urgently.

1. NHLS laboratories and virologist contact details

Groote Schuur EID lab, Western Cape (0214045254/ 0214045202)
Dr Marvin Hsiao (0214045200/ 0834451592 after hours)

Tygerberg EID lab, Western Cape (0219389355/ 0219389557)
Dr Jean Maritz (0219389057/ 0833633736 after hours)

Dora Nginza EID Lab, Eastern Cape (0414644635)
Dr Howard Newman (0413956152/ 0832646070 after hours)

Umtata EID lab, Eastern Cape (0413956152)
Dr Howard Newman (0413956152/ 0832646070 after hours)

Universitas EID lab, Free State and Northern Cape (0514053162)
Dr Daniel Morobadi (0514053162/ 0823134770 after hours)

Inkosi Albert Luthuli Central Hospital EID Lab, KwaZulu Natal (0312402800)
Dr Kerusha Govender (0312402822/ 0837799199 after hours)

Tshwane Academic Division EID lab, Gauteng (0123192257)
Dr Ahmad Haeri Mazanderani (0123192670/ 0826428609 after hours)

Charlotte Maxeke Johannesburg Academic EID Lab, Gauteng (0114898809)
Dr Lucia Hans (0114898408/ 0842068074 after hours)

Chris Hani Baragwanath Academic EID Lab, Gauteng (0114898708)
Dr Jeannette Wadula (0114898726/ 0828035699 after hours)

2. Contact details for treating paediatric clinicians; DCST paediatricians or paediatric nurses; PMTCT or HAST managers & co-ordinators

Every facility should have the contact details of clinicians or mentors who can assist with management of complex paediatric HIV cases. Alternatively, facilities should consult their NHLS HIV PCR laboratory virologists.

3. Telephonic helplines

Right to Care Paediatric HIV Helpline 083 3526642

National HIV & TB Health Care Workers Hotline 0800 212 506

COUNSELING SUGGESTIONS for HIV PCR indeterminate results

The mother/primary caregiver should be consulted regarding decisions about cART initiation. Any decision must consider the practical implications of where and how treatment will be continued. Infant feeding should be carefully discussed considering that breastfeeding improves outcome in HIV-infected infants. Maternal adherence to ART during breastfeeding should be stressed. All cases should urgently be brought to the attention of the relevant HIV clinic. Engagement of the family should be encouraged but the mother should guide the level of family involvement. Monitor the mother's well-being including adequate ART care and monitoring, TB screening and adequate psychosocial support. It is important to document discussions with the mother in the infant's bed letter and RTHB. The mother should have the clinic contact numbers and clinical course and decisions should be documented in the infant's road to health booklet to facilitate communication between different health care providers.

Where possible, to improve compliance, aim for continuity of care at a single facility preferably with a single healthcare worker.

The guiding principles of counseling in these cases should include:

1. The mother/primary caregiver must be involved with honest and frank information at every stage.

2. The message must be communicated that there is a team involved with the infant's care, that guidelines and resources exist to determine the final outcome. However, the length of this process is uncertain. Follow-up care and clear communication, both verbal and written, is critical especially for mobile mothers.

3. The team may not know the answer to the diagnostic dilemma at present but is aware how stressful this is and will undertake to find the solution in consultation with the mother and the necessary experts. At this stage it is critical that the follow-up care is monitored and tracked to reassure the mother/family that somebody is pursuing the problem. In the absence of a clear answer this should provide some level of relief.

4. A clear plan should be documented, communicated and adhered to. In the event of an unclear diagnosis despite all attempts to come to a clear solution, the last resort will be a monitored treatment interruption, if the infant is on cART, with follow-up testing at one month, three months, and three monthly thereafter for a minimum of 18 months off ART.

Note that these families need increased adherence support as they may be confused by the indeterminate results and the lack of a final confirmed diagnosis may contribute to poor adherence to ART.

References

1. South African National HIV Prevalence, Incidence and Behaviour Survey. HSRC 2014. http://www.hsrc.ac.za/en/research-outputs/view/6871
2. Millennium Development Goals. Country Report- South Africa 2013 http://www.za.undp.org/content/dam/south_africa/docs/Reports/The_Report/MDG_October-2013.pdf
3. 90 90 90 An ambitious treatment target to help end the AIDS epidemic. UNAIDS. 2014 http://www.unaids.org/sites/default/files/en/media/unaids/contentassets/documents/unaidspublication/2014/90-90-90_en.pdf
4. National Strategic Plan on HIV, STI's and TB 2012-2016 http://www.sahivsoc.org/upload/documents/National_Strategic_Plan_2012.pdf
5. Guidance on Couples' HIV Testing and Counselling including Antiretroviral Therapy for Treatment and Prevention in Serodiscordant Couples: Recommendations for a public health approach April 2012 http://www.sahivsoc.org/upload/documents/SOP%20for%20PCR%20indeterminates.pdf

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Caring Competence Accountability Integrity Responsiveness Respect