Western Cape Government

Health

PMTCT Clinical Guidelines Update

May 2013

CONTENTS

The Western Cape PMTCT Clinical Guidelines Update was adapted from the SA National PMTCT guidelines dated March 2013.

Acknowledgement goes to members of the PMTCT policy advisory group for their valuable input and comments.

FIGURES

TABLES

APPENDICES

ACRONYM GLOSSARY

3TC	Lamivudine
ART	Antiretroviral Treatment
ARV	Antiretrovirals
AZT	Zidovudine
CD4	Cluster of Differentiation 4
CM	Cryptococcal meningitis
CTX	Cotrimoxazole
CPT	Cotrimoxazole Prophylactic Treatment
DNA PCR	DNA Polymerase Chain Reaction
DR TB	Drug resistant TB
ELISA	Enzyme-linked immunosorbent assay
EFV	Efavirenz
FDC	Fixed dose combination
FTC	Emtricitabine
HCT	HIV Counselling and Testing
HIV	Human Immunodeficiency Virus
NVP	Nevirapine
MTCT	Mother-to-child transmission
PHC	Primary Health Care
PMTCT	Prevention of Mother-to-Child Transmission
RTHB	Road-to-Health Booklet
TB	Tuberculosis
TBM	TB meningitis
TDF	Tenofovir
VL	Viral Load

Western Cape Government
Health
BETTER TOGETHER.

ALGORITHM 1: PMTCT

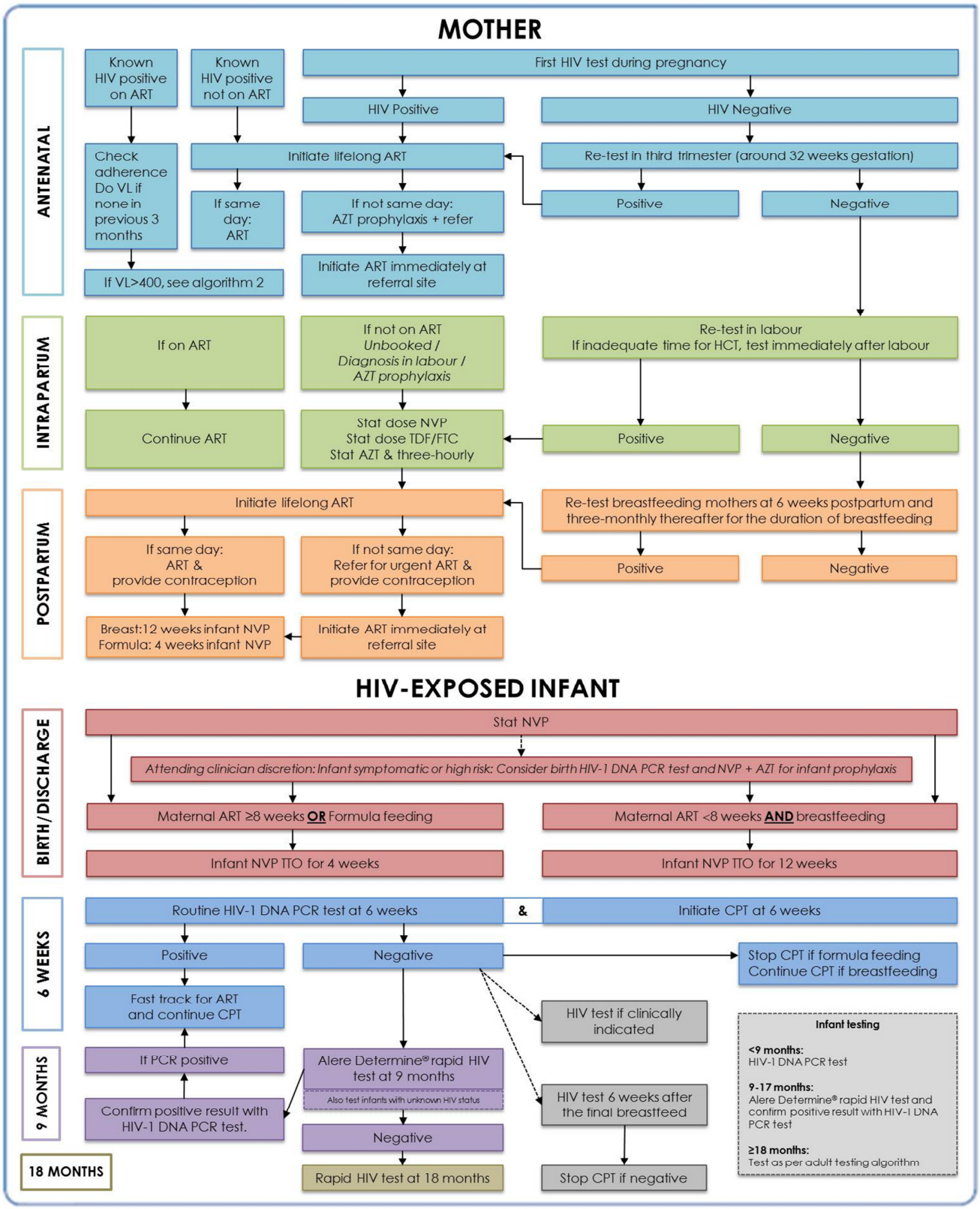


Figure 1. Algorithm 1: PMTCT

Figure 2. Algorithm 2: Viral Load monitoring and management during antenatal and postnatal care

(Algorithm developed by Drs G. Meintjies, R. Burton, J. Giddy & MSF doctors)

1. ART INITIATION DURING PREGNANCY AND BREASTFEEDING

All pregnant and breastfeeding HIV-infected women who are not on ART should initiate lifelong ART on the day of HIV diagnosis (new client) / at the first visit (known HIV not on ART), irrespective of CD4 count.

Certain medical conditions contraindicate same-day initiation and the following will apply:

Gestational age <12 weeks:
- Postpone ART initiation until 12 weeks unless treatment is clinically indicated and/or CD4 < 200 (these women should then be initiated on ART with Efavirenz).

TB patients with CD4 ≤50, or WHO stage IV disease [excluding TB meningitis (TBM) or Cryptococcal meningitis (CM)]:
- Initiate ART 2 weeks after starting TB treatment.

TB patients with CD4 >50 who have no WHO stage IV disease or markers of severity (BMI ≤18.5 or Hb ≤6.5):
- Initiate ART 2 to 10 weeks after starting TB treatment. Consult expert if in doubt.

Patients with TBM or CM:
- Initiate ART 4 to 6 weeks after starting TB treatment.

PREGNANT CLIENTS NOT ON ART

If lifelong ART can be provided at the antenatal clinic
- Initiate lifelong ART on the day of HIV diagnosis (do not wait for test results).

Do the following at the first visit (in addition to standard package of care):
- CD4 count and Serum Creatinine
- WHO staging
- TB symptom screening (repeat at every visit)
- STI screening
- HIV and ARV counselling
- Adherence counselling
- Assess for psychiatric illness
- Initiate ART immediately (do not wait for test results)
- Ask the mother to return in one week.

Do the following at the one week visit:
- Assess CD4 and Serum Creatinine results.
- Adherence counselling

If lifelong ART cannot be provided at the antenatal clinic (e.g. no pharmacy; no doctor or NIMART nurse):
- Initiate the client on **Zidovudine** (AZT) prophylaxis 300mg 12-hourly.
- Test Haemoglobin (Hb) concentration before commencing Zidovudine (AZT) prophylaxis.
  If Hb ≥8 g/dl: Initiate Zidovudine (AZT) prophylaxis.
  If Hb <8 g/dl: Do not initiate Zidovudine (AZT) prophylaxis. Refer for further management and urgent ART initiation.
- Refer to the nearest ART site for urgent initiation of ART. ART should be initiated within 7 days.
- Women referred for ART should be initiated immediately at their first visit to the referral site.

All clients referred for ART **must** receive AZT prophylaxis from the antenatal clinic **until** ART is commenced.

If the client returns to the antenatal clinic for more Zidovudine (AZT), find the reason why ART was not started and take steps to ensure urgent ART initiation.

Clients must be informed to **stop** Zidovudine (AZT) prophylaxis once they initiate ART.

Do the following at the first visit at the antenatal site (in addition to standard package of care):
- CD4 count and Serum Creatinine
- WHO staging
- TB symptom screening (repeat at every visit)
- STI screening
- HIV and ARV counselling
- Start on Zidovudine (AZT) prophylaxis and refer client for urgent ART initiation at the nearest ART site. Indicate on The Western Cape New Patient Referral to ART Services Form **(Appendix 1)** that CD4 count and Serum Creatinine have been done.

Do the following at the first visit at the site where ART will be issued:
- Assess for psychiatric illness
- Access CD4 and Serum Creatinine results from the NHLS website and assess.
- Initiate ART immediately (on the same day - do not wait for test results if not available yet).
- Adherence counselling

Clients who test HIV-positive at the birthing facility should be initiated on ART or referred for urgent ART once discharged depending on the capacity of the birthing facility.

BREASTFEEDING CLIENTS NOT ON ART

Initiation of maternal ART is especially urgent if the mother is breastfeeding.

If lifelong ART can be provided at the postnatal clinic
- Initiate lifelong ART on the day of HIV diagnosis.

If lifelong ART cannot be provided by the postnatal clinic (e.g. no doctor or NIMART nurse):
- Refer to the nearest ART site for urgent initiation of ART. ART should be initiated within 7 days.
- Postpartum women referred for ART should be initiated immediately at their first visit to the referral site.

Do the following at the postnatal clinic on the day of diagnosis (in addition to standard package of care):
- CD4 count and Creatinine clearance
- WHO staging
- TB symptom screening
- STI screening
- HIV and ARV counselling
- Adherence counselling
- Refer client for urgent ART initiation at the nearest ART site. Indicate on The Western Cape New Patient Referral to ART Services Form **(Appendix 1)** that CD4 count and Creatinine clearance have been done.

Do the following at the first visit at the site where ART will be issued:
- Assess for psychiatric illness
- Access CD4 and Creatinine clearance results from the NHLS website and assess.
- Initiate ART immediately (on the same day - do not wait for test results if not available yet).
- Adherence counselling

DRUG REGIMENS AND LABORATORY TESTS

The new South African antiretroviral guidelines recommend the use of Efavirenz (EFV) in pregnancy. Please refer to **Appendix 2** for more information.

Pregnant women

Drug regimens for pregnant women are based on the Western Cape Antiretroviral Treatment Guidelines 2013 (**Appendix 3** - Extract from *The Western Cape Antiretroviral Treatment Guidelines 2013: Adults and Adolescents*).

Table 1 indicates the laboratory tests and monitoring in pregnant women.

Table 1. Laboratory tests and monitoring in pregnant women

Prior to initiation of ART (Baseline)	Purpose
Hb and differential WCC: for patients provided with Zidovudine [AZT]	To detect anaemia; neutropenia
ALT: for patients initiating on Nevirapine [NVP]	To assess for liver dysfunction
Serum creatinine: for patients initiating on Tenofovir [TDF]	To detect renal insufficiency: if Serum Cr > 85 µmol/l: DO NOT use Tenofovir. Zidovudine and Lamivudine may be used: doses should be adjusted for renal impairment.
On ART	**Purpose**
CD4: at 1 year on ART. If CD4 < 200 cells/mm^3 repeat 6 monthly until two consecutive CD4's > 200 cells/mm^3	To monitor immune response to ART Stop prophylactic Cotrimoxazole after two consecutive CD4's > 200 cells/mm^3
<u>New ART client</u> VL at month 4, 8, and 12 of treatment and then 6 monthly until breastfeeding stopped. <u>Known HIV client on ART</u> • Do a viral load if not done (no result seen) in the previous 3 months. • VL 6 monthly for duration of pregnancy and breastfeeding • Do a VL if in doubt about adherence or suspect patient has defaulted treatment. <u>All</u> Do a VL at 34 weeks if no VL has been done in the last 3 months. If on DR TB treatment: VL 6 monthly until DR TB treatment completed	To monitor response to treatment and identify treatment failures. VL is the best predictor of transmission antenatally, during labour and while breastfeeding. Ensuring an undetectable VL throughout pregnancy & breastfeeding is essential to eliminate MTCT, which is the reason for more frequent VL monitoring than in the general population. Attempt to align VL tests with antenatal / postnatal visits, and also consider gestational age and timing of delivery e.g. if woman likely to deliver at or just before month 4 on ART, do VL in late pregnancy. To ensure that women who say they are on ART at booking have not defaulted.
Figure 2 (Algorithm 2) depicts detailed VL monitoring and management during antenatal and postnatal care.	

ALT: If on Nevirapine [NVP] or Efavirenz [EFV] **and** develops rash or symptoms of hepatitis If on TB treatment and Lopinavir/ritonavir	To identify Nevirapine [NVP] or Efavirenz [EFV] toxicity At weekly intervals, check ALT. If ALT < 50 on 4 tablets 12 hourly: 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.
Hb and differential WCC: at month 1, 2, 3 and 6 if on Zidovudine [AZT]	To identify Zidovudine [AZT] toxicity
Fasting cholesterol and triglycerides: baseline on initiating Lopinavir / ritonavir [LPV/r]. Then at month 4, month 12 and then annually	To identify Lopinavir / ritonavir [LPV/r] toxicity
Hep B sAg[see under 2nd line treatment]	Patients on Tenofovir [TDF] and Emtricitabine [FTC] or Lamivudine [3TC] changing to medication where **one or both** of these medicines may be stopped.

Postpartum women

Laboratory tests **and** drug regimens for postpartum women should be managed according to The Western Cape Antiretroviral Treatment Guidelines 2013 (**Appendix 3** - Extract from *The Western Cape Antiretroviral Treatment Guidelines 2013: Adults and Adolescents*).

Viral load testing for breastfeeding women is more frequent than for standard adult ART monitoring (Table 2).

Table 2. Viral load testing for breastfeeding women

New ART client VL at month 4, 8, and 12 of treatment and then 6 monthly until breastfeeding stopped. Known HIV client on ART • Do a viral load if not done (no result seen) in the previous 3 months. • VL 6 monthly for duration of pregnancy and breastfeeding • Do a VL if in doubt about adherence or suspect patient has defaulted treatment.	To ensure optimal viral suppression prior to delivery. Attempt to align VL tests with antenatal / postnatal visits.
Figure 2 (Algorithm 2) depicts detailed VL monitoring and management during antenatal and postnatal care.	

COUNSELLING

Do HIV and ARV counselling on the day of HIV diagnosis.
Clients should receive on-going adherence counselling as part of the ART programme.

2. ANTENATAL CARE

HIV-POSITIVE CLIENTS

New HIV diagnosis / Known HIV-positive client not on ART
- Initiate lifelong ART as described in Section 1.

Known HIV-positive clients on ART
- Check for adherence (e.g. green HIV card, Tier.net, eKapa, NHLS result system) and do a viral load if it was not done / no result seen for the previous 3 months.
- If the client's ART regimen is FDC compatible (TDF, 3TC, EFV or TDF, FTC, EFV), switch client to the FDC.
- If the client's ART regimen is not FDC compatible (e.g. AZT/3TC/EFV or d4T/3TC/EFV or TDF/3TC/NVP), leave the client's ART regimen unchanged.

HIV-NEGATIVE CLIENTS

All clients who tested HIV-negative at their initial test should be re-tested for HIV in the third trimester (at around 32-weeks gestation).

If HIV positive
- Initiate lifelong ART as described in Section 1.

If HIV negative
- Inform the client that she will be re-tested for HIV in labour.

3. INTRAPARTUM CARE

HIV-POSITIVE CLIENTS

Clients on ART
- Check for adherence (e.g. green HIV card, Tier.net, eKapa, NHLS result system) and do a viral load if it was not done / no result in the previous 3 months.
- Continue ART during labour. No additional drugs are required.

Clients not on ART
(e.g. unbooked clients, clients on AZT prophylaxis, HIV diagnosis in labour)
- At presentation in labour give a stat dose of **Nevirapine** 200mg (sdNVP), **Truvada®** (Tenofovir (TDF) 300mg / Emtricitabine (FTC) 200mg) and oral **Zidovudine** (AZT) 300mg.
- Give oral **Zidovudine** (AZT) 300mg every three hours during labour until delivery.

Instrumentation
- Artificial rupture of membranes should not be undertaken if progress of labour is adequate.
- Invasive procedures such as fetal scalp blood sampling or fetal scalp heart monitoring should be avoided.
- Unnecessary episiotomies should be avoided.

HIV-NEGATIVE CLIENTS / UNKNOWN HIV STATUS

All clients whose HIV status is unknown should be tested in labour. Clients who previously tested HIV-negative should also be tested in labour if there is adequate time for HIV counselling and testing (HCT) by midwives.

If there is inadequate time for HCT in labour, HIV testing should be offered immediately after delivery.

If the client tests HIV positive in labour
- Immediately give a stat dose of **Nevirapine** 200mg (sdNVP), **Truvada®** (Tenofovir (TDF) 300mg / Emtricitabine (FTC) 200mg) and oral **Zidovudine** (AZT) 300mg.
- Give oral **Zidovudine** (AZT) 300mg every three hours during labour until delivery.

If HIV negative
- Inform the client that she will be re-tested for HIV at six-weeks postpartum.

4. POSTPARTUM CARE OF THE MOTHER

HIV-POSITIVE MOTHERS

Before discharge:

Mothers on ART
- Check for adherence (e.g. green HIV card, Tier.net, eKapa, NHLS result system) and do a viral load if it was not done / no result in the previous 3 months.
- Continue lifelong ART.
- Provide appropriate contraception.

Mothers not on ART
(e.g. unbooked clients, clients on AZT prophylaxis, HIV diagnosis in labour)
- Initiate lifelong ART as described in Section 1, irrespective of feeding choice.
- Initiation of ART is especially urgent if breastfeeding.
- Provide appropriate contraception.

HIV-NEGATIVE BREASTFEEDING MOTHERS

Perform an HIV test at 6 weeks postpartum and three-monthly thereafter for the duration of breastfeeding.
- It is advised to link the three-monthly HIV test to the mother's three-monthly depot contraception schedule where applicable.

If the mother tests HIV positive

Mother
- Initiate lifelong maternal ART urgently as described in Section 1.
- Provide appropriate contraception.

Infant
- Do infant HIV-1 DNA PCR test

If PCR positive
- Fast track for ART.
- Do a baseline viral load but do not delay ART initiation while waiting for the result.

If PCR negative and breastfeeding continued
- Provide Nevirapine (NVP) TTO to complete a total of twelve weeks prophylaxis (until breastfeeding mother is established on ART and virologically suppressed) and explain to the mother how it should be administered (Table 3).

If PCR negative and breastfeeding discontinued
- Provide Nevirapine (NVP) TTO to complete a total of four weeks prophylaxis and explain to the mother how it should be administered (Table 3).

Table 3. Nevirapine (NVP) doses for prophylaxis after six weeks of age

	Age	Daily Dosage	Volume
Nevirapine (NVP) syrup (10mg/ml)	If 6 weeks to 6 months	20mg	2ml
	If 6 months to 9 months	30mg	3ml
	If 9 months to 12 months	40mg	4ml

5. CARE OF HIV-EXPOSED INFANTS

If symptomatic or classified as high risk (attending clinician discretion)

If NVP resistance likely or no prelabour ARVs, consider combining AZT and NVP for infant prophylaxis. Discuss further management with an expert.

Perform an HIV-1 DNA PCR test soon after birth.

If PCR positive
- Fast track for ART.
- Do a baseline viral load but do not delay ART initiation while waiting for the result.

If PCR negative
- Repeat the HIV-1 DNA PCR test at 6 weeks.

Abandoned infants / Orphans
- Immediately perform a rapid HIV test to determine if the infant was exposed to HIV.
- If the rapid HIV test is positive, perform an HIV-1 DNA PCR test and manage as above.
- These infants qualify for donated expressed breast milk (if available) or formula feeding.

AT BIRTH

Give all infants oral Nevirapine (NVP) urgently after birth (within 72 hours) (Table 4).

Table 4. Nevirapine (NVP) doses for prophylaxis at birth

	Birth Weight	Dosage	Volume
Nevirapine (NVP) syrup (10mg/ml)	<2.0kg	2mg/kg	0,2 ml/kg
	2.0 – 2.5kg	10mg	1ml
	>2.5kg	15mg	1.5ml

IN HEALTH FACILITY

Provide daily NVP as per dosing schedule (or other ARV prophylaxis regimen under expert guidance) (Tables 5 and 6).

AT DISCHARGE

Formula fed infants

At discharge, provide Nevirapine (NVP) TTO (or other ARV prophylaxis regimen under expert advice) to complete a total of four weeks postnatal prophylaxis and explain to the mother how it should be administered (Table 5).

Breastfed infants

If mother was on ART for ≥8 weeks prior to labour

- At discharge, provide Nevirapine (NVP) TTO (or other ARV prophylaxis regimen under expert advice) to complete a total of four weeks postnatal prophylaxis and explain to the mother how it should be administered (Table 5).

Table 5. Nevirapine (NVP) doses for prophylaxis in the first four weeks of life

	Birth Weight	Age	Daily Dosage	Volume
Nevirapine (NVP) syrup (10mg/ml)	<2.0kg	Birth to 2 weeks	2mg/kg	0,2 ml/kg
		2 to 4 weeks	4mg/kg	0,4 ml/kg
	2.0 – 2.5kg	Birth to 4 weeks	10mg	1ml
	>2.5kg	Birth to 4 weeks	15mg	1.5ml

If mother was on ART for <8 weeks prior to labour
(Includes new maternal HIV diagnosis in labour)

- If mother not yet on ART, initiate ART urgently as described in Section 1.
- At discharge, provide Nevirapine (NVP) TTO (or other ARV prophylaxis regimen under expert advice) to complete a total of twelve weeks postnatal prophylaxis and explain to the mother how it should be administered (Table 6).

Table 6. Nevirapine (NVP) doses for prophylaxis in the first twelve weeks of life

	Birth Weight	Age	Daily Dosage	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
		6 to 12 weeks*	20mg	2ml
	2.0 – 2.5kg	Birth to 6 weeks	10mg	1ml
		6 to 12 weeks	20mg	2ml
	>2.5kg	Birth to 6 weeks	15mg	1.5ml
		6 to 12 weeks	20mg	2ml

*Consider dose of 4mg/kg if still an in-patient and weighs <2kg at 6-12 weeks.

AT SIX WEEKS

Routine HIV-1 DNA PCR test

- Perform an HIV-1 DNA PCR test and review the result as soon as possible.

If PCR positive

- Fast track for ART.
- Do a baseline viral load but do not delay ART initiation while waiting for the result.

If PCR negative

- Repeat HIV testing at 9 months and at any time if ill.

Cotrimoxazole Prophylactic Treatment (CPT)

- Initiate Cotrimoxazole Prophylactic Treatment (CPT) at 6 weeks of age (Table 7). If breastfeeding and 6 week PCR is negative, continue Cotrimoxazole Prophylactic Treatment (CPT) until HIV infection is excluded by HIV testing 6 weeks after final breastfeed.
- If formula feeding and 6-week PCR is negative then stop Cotrimoxazole Prophylactic Treatment (CPT).

Table 7. Cotrimoxazole Prophylactic Treatment (CPT) dosing table

	Weight	Daily Dosage
Cotrimoxazole (CTX) syrup (40/200mg/5ml) or tablet (80/400mg)	<5kg	2.5 ml
	5 - <14kg	5 ml or ½ tablet
	14kg - <30kg	10 ml or 1 tablet
	>30 kg	2 tablets

AT 9 MONTHS

Routine HIV testing

Perform HIV testing at 9 months in:

- All HIV-exposed infants not on ART.
- Infants with unknown HIV status (particularly important to those whose mothers were not tested for HIV during pregnancy or who were not enrolled on the PMTCT programme) (Figure 3).

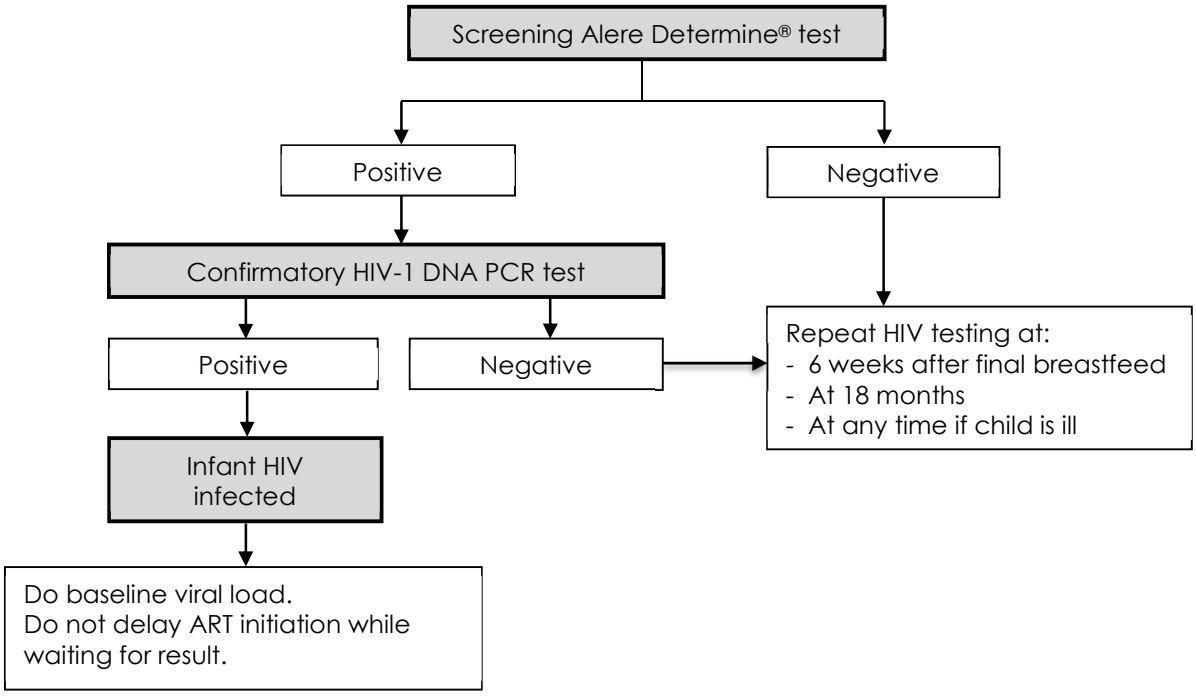


Figure 3. Testing algorithm at nine months

AT 18 MONTHS

Routine HIV testing

Perform HIV testing at 18 months in all HIV-exposed infants not on ART (Figure 4).

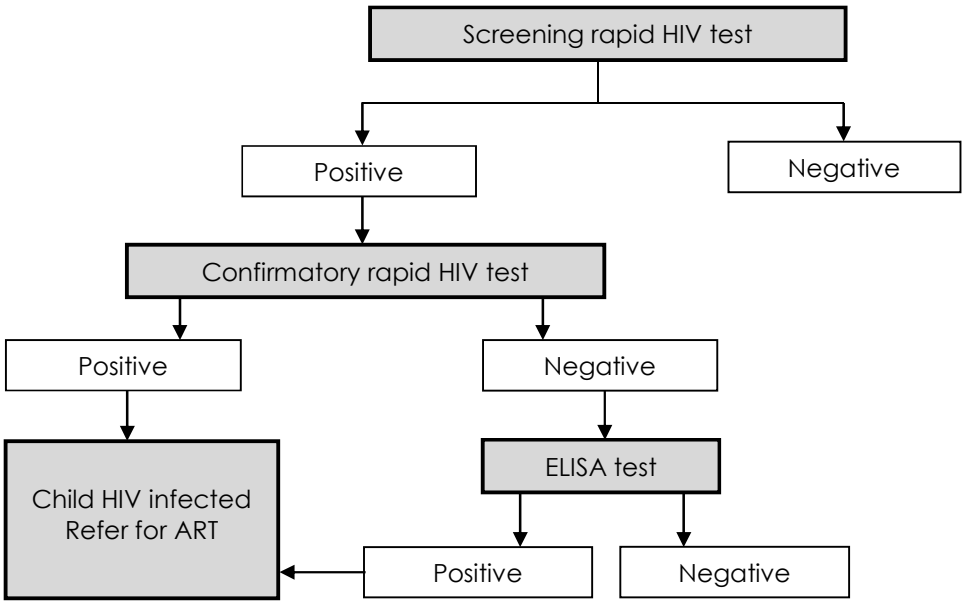


Figure 4. Testing algorithm at eighteen months

SIX WEEKS AFTER FINAL BREASTFEED

Perform an HIV test six weeks after the final breastfeed.

<9 months:
HIV-1 DNA PCR test
9-17 months:
Alere Determine® rapid HIV test and confirm positive result with HIV-1 DNA PCR test

If PCR positive
- Fast track for ART.
- Do a baseline viral load but do not delay ART initiation while waiting for the result.

If PCR negative
- Discontinue Cotrimoxazole Prophylactic Treatment (CPT).

IF CLINICALLY INDICATED

Perform an HIV test in infants who have recurrent infections / illnesses (e.g. chest infections, gastroenteritis) or who are not gaining weight.

<9 months:
HIV-1 DNA PCR test
9-17 months:
Alere Determine® rapid HIV test and confirm positive result with HIV-1 DNA PCR test
≥18 months:
Test as per adult testing algorithm

If HIV positive
- Fast track for ART.
- Do a baseline viral load but do not delay ART initiation while waiting for the result.

6. INFANT FEEDING

HIV-EXPOSED INFANTS

- Clients must receive on-going infant feeding counselling throughout antenatal care, in labour, following delivery and at post-natal follow up.

- Infant feeding counselling should be initiated by introducing the mother to infant feeding options and making her aware of the risks and benefits of all options. The mother should be supported to make an informed and appropriate feeding choice suitable to her circumstances. Ensure that the infant feeding choice is practiced correctly.

For detailed infant feeding counselling guidelines, please refer to *Circular H166/2012: Infant feeding counselling guideline*.

For criteria for safe infant feeding by HIV-infected mothers, please refer to **Appendix 4** (Extract from *Circular H186/2012: Criteria for Safe Infant Feeding by HIV-infected Mothers*)

- For breastfeeding mothers, encourage and support exclusive breastfeeding for the first six months of life, and continued breastfeeding thereafter with appropriate complementary feeding until twelve months of age. Mixed feeding during the first six months of life should be strongly discouraged.

Exclusive breastfeeding:
Nothing but breast milk, not even water. Vitamin supplementation and prescribed medicines are allowed.

Mixed feeding:
Giving breast milk and water or other fluids, formula milk or food.

- The Western Cape Province will continue to provide formula milk (until the age of 6 months) if a mother chooses to formula feed after receiving infant feeding counselling on appropriate feeding choices.

HIV-POSITIVE INFANTS

- Encourage breastfeeding for 2 years and longer while continuing infant ART.

7. RECORDING OF INFORMATION

The following documents should be completed in full to enable successful linkage to care and monitoring and evaluation of the PMTCT programme:

STATIONERY

- HCT Consent Form
- ART stationery
- PMTCT Discharge Letter **(Appendix 5)**
- Maternity Case Record including the new PMTCT Check List

It is important that the duplicate, perforated PMTCT check list in the Maternity Case Record is also completed in full, torn out and given to the mother to take to the baby follow-up visits.

- Road-to-Health Booklet (RTHB) including page 7 and 8

It is important that healthcare workers are diligent in completing this record at every point that an infant and young child is seen at a health facility. Information regarding HIV exposure and PMTCT interventions are CRITICAL for the continued management of mothers and infants.

REGISTERS

- Antenatal HIV Counselling and Testing register
- PMTCT Labour ward register
- PMTCT Baby follow-up register

- HIV Counselling and Testing Register
  - HIV test in labour
  - HIV test if breastfeeding
  - Infant test at 9 months
  - Infant test at 18 months
  - Partners of pregnant women

Appendix 1: The Western Cape New Patient Referral to ART Services Form

Western Cape New Patient Referral to ARV Services Form

First Name		Folder #:	
Surname		Phone #:	
DOB	……. /…… /…… Sex: M / F	Address:	
ID Number			

Please consider the patient for: (please tick/circle appropriate response and provide details)	☐ FAST TRACK initiation of ART on the basis of: Pregnant/breastfeeding TB with CD4<50 CD4<200 Stage 4 Child < 1 year
	☐ Routine initiation of ART
	☐ Assessment of eligibility for ART

HIV/ART information

Tested HIV+ on … / ... / …	Latest CD4: … / ... / ... Result: _____ Specimen sent: … / ... /...	WHO Stage:
Previous ART YES NO If yes, please specify regimen and Start and Stop date	Regimen: _____ Start Date: … / ... / … Stop Date: … / … /...	
Previous PMTCT YES NO If yes, please specify regimen and Start and Stop date	Regimen:_____ Start Date: … /... / ... Stop Date: … /... /...	

TB information

Current TB: YES NO Type: PTB EPTB Site:_____	TST done: YES NO Date: … / … / … Result: _____
TB Treatment : Start Date: … / … / … Planned Stop Date: … / … / …	IPT Treatment: Start Date: … / … / … Planned Stop Date: … / … / …

Recent TB Investigation

Sputum: Date: … / ... / … Lab No: Result:	Sputum: Date: … / ... / … Lab No: Result:
Genexpert: Date: … / ... / … Result: *Negative* *Positive*	Culture: Date: … / ... / … Lab No: Result:
Drug Sensitivity Test: Date: : … / ... / … Comment: _____	

Medical History

Please include:

- Previous TB diagnoses and dates _____
- Past or current opportunistic infections _____
- Medical conditions _____
- Recent hospital admissions _____
- Relevant social history _____

Current Medication	_____ _____ _____

Allergies: YES NO If yes, please specify:		
RPR: Date: … / ... / ... Result:		Treatment:
Pap smear: Date: … /… / ... Result:		
Contraception: YES NO If yes, please specify method:		
Referring facility	Name: Address/Phone Number: Facility Referred to:	Facility Stamp:
Referring CLINICIAN	Name:	Signature: Date:

NB: Patient to please bring hospital cards (including TB Card) and all medication to initial visit

Appendix 2: Press release on the safety of Efavirenz in pregnancy

Drug safety in pregnancy is an important public health concern, but reliable data is difficult to obtain as pregnant women are excluded from drug trials of almost all drugs. Efavirenz exposure in early pregnancy resulted in severe birth defects in primates and isolated case reports in humans reported similar abnormalities. For this reason Efavirenz is not recommended for use in pregnant women by regulatory authorities, including the Medicines Control Council. However, there is recent reassuring human data on the safety of Efavirenz in pregnancy. In 2011 a meta-analysis found no increased risk of birth defects in 1,290 live births from mothers who were exposed to Efavirenz compared with 8,122 live births from mothers who were exposed to other antiretroviral drugs in the first trimester of pregnancy.

Nevirapine, which is the alternative drug to Efavirenz, is considered to be safe in pregnancy, but it is associated with life threatening hypersensitivity reactions. A meta-analysis of the safety of Nevirapine in pregnancy has shown that hypersensitivity reactions to Nevirapine occur more commonly than in women who are not pregnant. Hypersensitivity reactions also occur much more commonly in women starting Nevirapine with higher CD4 counts. In the new South African guidelines all pregnant women are offered combination antiretroviral therapy, irrespective of their CD4 count. Therefore continued recommendation of Nevirapine will put pregnant women at high risk of severe hypersensitivity reactions.

The meta-analysis showing no increased risk of birth defects with exposure to Efavirenz in early pregnancy, together with serious safety concerns about Nevirapine, were carefully considered by an expert group (including experts from the World Health Organization) advising the Department of Health. The new South African antiretroviral guidelines recommend the use of Efavirenz in pregnancy. The routine use of Nevirapine in pregnancy is no longer recommended because of serious safety concerns. Nevirapine is still available for patients who are unable to tolerate Efavirenz or in whom Efavirenz is contraindicated.

There is insufficient evidence to categorically state that Efavirenz does not cause birth defects. Rare birth defects caused by drugs can only be excluded with very large studies. For this reason the Department of Health has undertaken to establish pregnancy registries to document birth defects in HIV-infected women exposed to antiretroviral therapy as part of pharmacovigilance activities of the Department of Health. The policy to use Efavirenz in pregnancy will be reviewed if data from the South African and other pregnancy registers indicate that Efavirenz does cause birth defects.

References

Ford N, Calmy A, Mofenson L. Safety of efavirenz in the first trimester of pregnancy: an updated systematic review and meta-analysis. *AIDS*, 2011, 25(18):2301–2304.

Bera E, Mia R. Safety of nevirapine in HIV-infected pregnant women initiating antiretroviral therapy: a systematic review and meta-analysis. *SAMJ* 2012;102:855-859.

World Health Organization. Technical update on treatment optimization: use of efavirenz during pregnancy: a public health perspective. June 2012.

Appendix 3: Extract: The Western Cape Antiretroviral Treatment Guidelines 2013: Adults and Adolescents

A) STANDARDISED WESTERN CAPE ART REGIMENS FOR ADULTS AND ADOLESCENTS

1st Line		
All new patients needing treatment, including pregnant women	Tenofovir [TDF] daily **+** Emtricitabine [FTC] (or Lamivudine [3TC] daily **+** Efavirenz [EFV] daily fixed dose combination preferred	<u>Adolescents - new:</u> TDF 300mg daily if ≥15 years of age **AND** ≥40kg **AND** eGFR is ≥ 80 <u>Adolescents – on treatment:</u> switch to TDF 300mg daily if ≥15 years of age **AND** ≥40kg **AND** VL < 400 copies/ml **IF** eGFR is ≥ 80
Contraindications to Efavirenz [EFV]	Tenofovir [TDF] daily **+** Emtricitabine [FTC] (or Lamivudine [3TC] daily **+** Nevirapine [NVP] twice daily	Use NVP based regimen in patients with significant psychiatric co-morbidity or intolerance to EFV where the neuro-psychiatric toxicity may impair daily functioning, 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
Contraindication to Tenofovir [TDF]	Zidovudine [AZT] daily **+** Lamivudine [3TC] daily **+** Efavirenz [EFV] daily **OR** Nevirapine [NVP] twice daily	Renal disease [Cr Cl ≤ 50 ml/min] or the concurrent use of other nephrotoxic drugs e.g. aminoglycosides [kanamycin] Pregnant women: Cr > 85µmol/l
Contraindication to Tenofovir [TDF] and Zidovudine [AZT]	Stavudine [d4T] twice daily **+** Lamivudine [3TC] twice daily **+** Efavirenz [EFV] daily **OR** Nevirapine [NVP] twice daily	Renal disease [Cr Cl ≤ 50 ml/min] or the concurrent use of other nephrotoxic drugs e.g. aminoglycosides [kanamycin] and anaemia [Hb ≤ 8g/dl: use Zidovudine 200mg bd; Hb ≤ 6.5 g/dl: change medicine]
Contraindication to Tenofovir [TDF]; Zidovudine [AZT] and Stavudine [d4T]	Abacavir [ABC] twice daily **+** Lamivudine [3TC] twice daily **+** Efavirenz [EFV] daily **OR** Nevirapine [NVP] twice daily	Renal disease [Cr Cl ≤ 50 ml/min] or the concurrent use of other nephrotoxic drugs e.g. aminoglycosides [kanamycin]; anaemia [Hb ≤ 8g/dl: use Zidovudine 200mg bd; Hb ≤ 6.5 g/dl: change medicine]; peripheral neuropathy; hyperlactataemia; lipoatrophy [circular H34 2012: submit motivation]
Currently on d4T-based regimen	Tenofovir [TDF] daily **+** Emtricitabine [FTC] (or Lamivudine [3TC) daily **+** Efavirenz [EFV] daily	If patients experience, or are at high risk of, toxicity (high BMI or pregnant). Switch to TDF if virologically suppressed and the patient's creatinine clearance is normal

<table>
<tr><th colspan="3">2nd Line</th></tr>
<tr><td>Management of virological failure</td><td colspan="2">If plasma viral load [VL] > 1 000 copies/ml:
- Check adherence, compliance, tolerability, drug-drug interactions and assess any psychological issues.
- Repeat VL test within 3 months.
- If patient pregnant: repeat VL test earlier: between 1 and 2 months and support adherence if suspect non adherent

If plasma VL confirmed > 1 000 copies/ml change to second line therapy
<u>Patients on Tenofovir and Emtricitabine [or Lamivudine]:</u>
- Check Hepatitis B status prior to changing regimen
- If HepB sAg positive: maintain patients on Tenofovir and Emtricitabine [or Lamivudine]
Suggested regimen would be: TDF + AZT + FTC [or 3TC] + LPV/r</td></tr>
<tr><td>Failing on a Tenofovir [TDF] -based 1st line regimen</td><td>Zidovudine [AZT] twice daily +
Lamivudine [3TC] twice daily +
Lopinavir / ritonavir [LPV/r] twice daily</td><td></td></tr>
<tr><td>Failing on a Stavudine [d4T] or Zidovudine [AZT] based 1st line regimen</td><td>Tenofovir [TDF] +
Lamivudine [3TC] +
Lopinavir / ritonavir [LPV/r] twice daily</td><td>LPV/r may increase the levels of TDF: monitor for TDF side effects</td></tr>
<tr><td>Contraindication to Tenofovir [TDF]; Zidovudine [AZT] and Stavudine [d4T]</td><td>Abacavir [ABC] twice daily +
Lamivudine [3TC] twice daily +
Lopinavir / ritonavir [LPV/r] twice daily</td><td>Renal disease [Cr Cl ≤ 50 ml/min] or the concurrent use of other nephrotoxic drugs e.g. aminoglycosides [kanamycin]; anaemia [Hb ≤ 8g/dl: use Zidovudine 200mg bd; Hb ≤ 6.5 g/dl: change medicine]; peripheral neuropathy; hyperlactataemia; lipoatrophy [circular H34 2012: submit motivation]</td></tr>
<tr><td>Lopinavir / ritonavir [LPV/r] related adverse effects:
Hypertriglyceridaemia: fasting triglycerides > 5mmol/l
Cardiovascular event risk > 20%
Severe hypercholesterolaemia: Total Cholesterol > 7.5mmol/l
Established clinical cardiovascular disease
Severe GIT side effects: > 6 weeks</td><td>Switch Lopinavir / ritonavir [LPV/r] to

Atazanavir / ritonavir [ATV/r]</td><td>No motivation required

Refer to Circular H148 2011</td></tr>
<tr><th colspan="3">Third line</th></tr>
<tr><td>Failing any 2nd line regimen: A provincial policy will be forthcoming</td><td colspan="2">Specialist referral: Should be managed by an infectious disease specialist on the basis of genotype resistance testing. Most likely regimen may include one or more of the following: Raltegravir, Darunavir or Etravirine.</td></tr>
</table>

B) STANDARDIZED WESTERN CAPE MONITORING FOR ADULTS AND ADOLESCENTS WITH HIV

At initial Diagnosis of HIV	Purpose
Confirm HIV status	Ensure that Western Cape testing algorithm has been followed
Do CD4 count and WHO clinical staging if HIV positive	To assess eligibility for ART To assess eligibility for fast-tracking
Screen for pregnancy or ask if planning to conceive	To identify women who need ART
Screen for TB symptoms	To identify TB/HIV co-infection [refer to WC TB screening tool]
Mantoux test [TST]	Identify need for IPT
CLAT: All HIV + patients with an initial CD4 < 100 cells/mm^3	Identify patients who required cryptococcal meningitis prophylaxis with fluconazole
Prior to initiation of ART (Baseline)	**Purpose**
Hb and differential WCC: for patients initiating on Zidovudine [AZT]	To detect anaemia; neutropenia
ALT: for patients initiating on Nevirapine [NVP]	To assess for liver dysfunction
Serum creatinine and creatinine clearance: for patients initiating on Tenofovir [TDF] If pregnant: serum creatinine level	To detect renal insufficiency: if CrCl ≤ 50: DO NOT use Tenofovir. Zidovudine and Lamivudine may be used: doses should be adjusted for renal impairment. Should be ≤ 85 µmol/l
On ART	**Purpose**
CD4: at 1 year on ART. If CD4 < 200 cells/mm^3 repeat 6 monthly until two consecutive CD4's > 200 cells/mm^3	To monitor immune response to ART Stop prophylactic cotrimoxazole and fluconazole after two consecutive CD4's > 200 cells/mm^3
VL: at month 4, month 12 and then annually If on DR TB treatment: VL 6 monthly until DR TB treatment completed If pregnant AND breastfeeding: at month 4, month 8, month 12 and then 6 monthly until breastfeeding stopped. Do a VL at 34 weeks if no VL has been done in the last 3 months.	To monitor response to treatment and identify treatment failures To ensure optimal viral suppression prior to delivery. Attempt to align VL tests with antenatal / postnatal visits
ALT: If on Nevirapine [NVP] or Efavirenz [EFV] **and** develops rash or symptoms of hepatitis If on TB treatment and lopinavir/ritonavir	To identify Nevirapine [NVP] or Efavirenz [EFV] toxicity At weekly intervals, check ALT and increase LPV/r to 3 and then 4 tablets 12 hourly if ALT < 50 If ALT < 50 on 4 tablets 12 hourly: 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.
Hb and differential WCC: at month 1, 2, 3 and 6 if on Zidovudine [AZT]	To identify Zidovudine [AZT] toxicity
Creatinine clearance: at month 1; 4; 12 and then every 12 months if on Tenofovir [TDF]	To identify Tenofovir [TDF] toxicity. If < 16 years: the following formula should be used: $GFR = \frac{\text{height [cm]} \times 40}{\text{creatinine [µmol/l]}}$ If > 16 years: use adult weight-based formula for GFR $\text{GFR [ml/min]} = \frac{(140 - \text{age}) \times \text{Wt (kg)}}{\text{Scr (µml /L)}}$ Females: multiply GFR by 0.85
Fasting cholesterol and triglycerides: baseline on initiating Lopinavir / ritonavir [LPV/r]. Then at month 4, month 12 and then annually	To identify Lopinavir / ritonavir [LPV/r] toxicity
Hep B sAg[see under 2nd line treatment]	Patients on Tenofovir [TDF] and Emtricitabine [FTC] or Lamivudine [3TC] changing to medication where **one or both** of these medicines may be stopped.

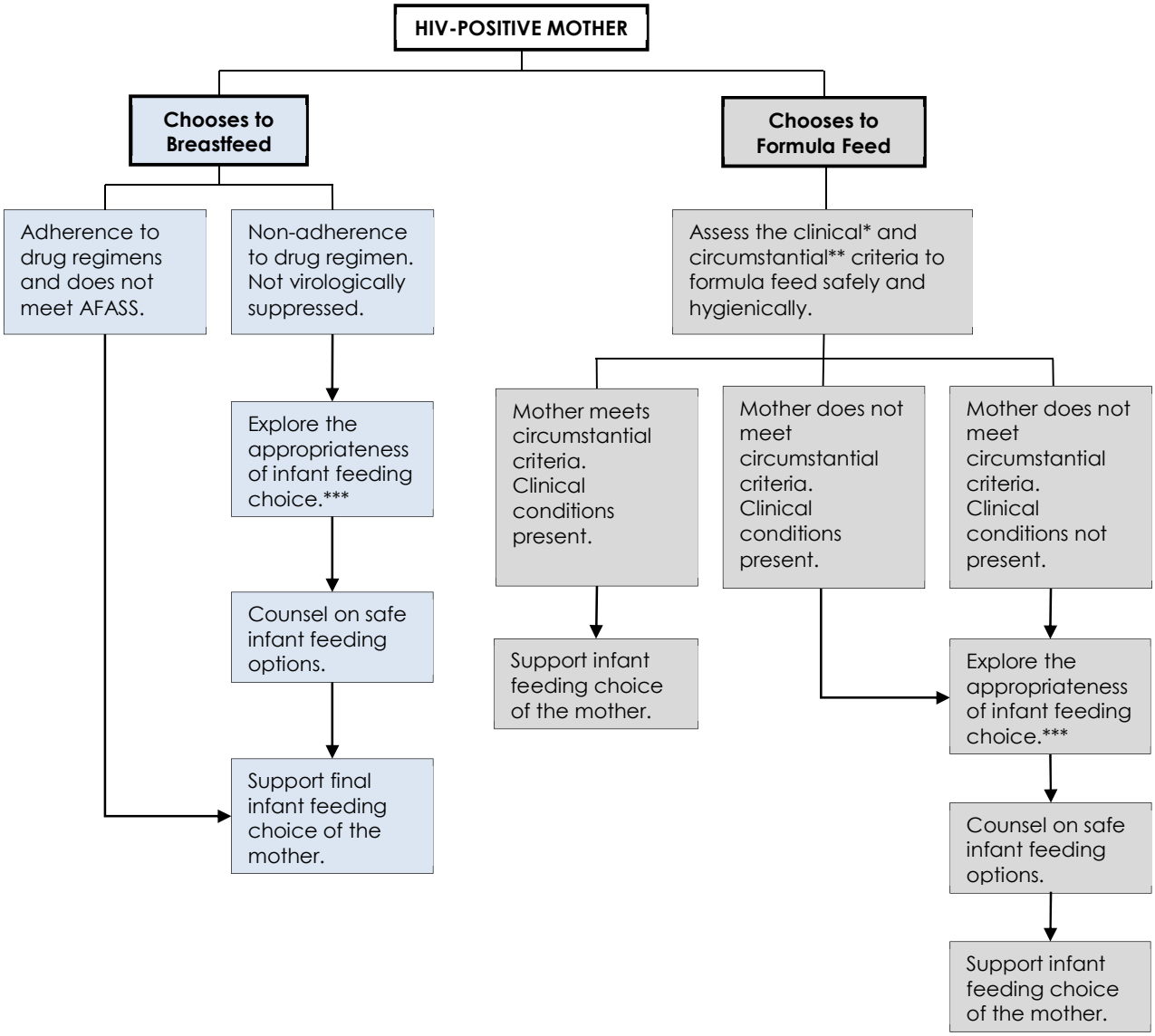
C) INDICATIONS FOR REFERRAL TO A DOCTOR:

- eGFR less than 60 ml/min
- Hb less than 8 g/dl
- Poor response to TB treatment
- Clinical signs of possible meningitis: e.g. confusion; headaches
- Psychiatric illness e.g psychosis, schizophrenia

Appendix 4: Extract: Circular H186/2012: Criteria for Safe Infant Feeding by HIV-infected Mothers: Algorithm.

Exclusive Breastfeeding for the first 6 months of life is the optimal feeding choice and cornerstone of child survival!

ALGORITHM FOR SUPPORTING SAFE AND APPROPRIATE INFANT FEEDING BY HIV-INFECTED MOTHERS



Please note: Women who are on 2nd line ART and are not virologically suppressed (either due to non-adherence or true resistance to 2nd line drugs) do not qualify to breastfeed and should receive infant formula for the first six months of the infant's life and subsequently in three monthly increments.

* Clinical conditions: Client is not adhering to the drug regime and / or client is not virologically suppressed (on HAART or AZT for <3 months) and / or client on 2nd line ART and is not virologically suppressed.
**Circumstantial criteria for safe replacement feeding: please refer to section A of the circular.
***Refer to circular H166/2012 (Infant Feeding Counselling Guideline).

Appendix 5: PMTCT infant discharge letter

Western Cape Government
Health

PMTCT infant discharge letter
(to be given to patient)

Dear Colleague

INFANT SURNAME: …… INFANT FIRST NAME: ……

INFANT HOSPITAL NUMBER:…… DOB: ……/……/……

Has been discharged from …… (delivery facility) on: …….. (date)

Mother started ART _____ weeks prior to delivery. The infant has been discharged on:

Daily Nevirapine (NVP) prophylaxis for 4 weeks / 12 weeks (please circle) as per the 2013 PMTCT Clinical Guidelines Update.

	Birth Weight	Age	Daily Dosage	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
		6 to 12 weeks	20mg	2ml
	2.0 – 2.5kg	Birth to 6 weeks	10mg	1ml
		6 to 12 weeks	20mg	2ml
	>2.5kg	Birth to 6 weeks	15mg	1.5ml
		6 to 12 weeks	20mg	2ml

Feeding method at discharge: Breastfeeding ☐ Formula feeding ☐

Please perform an HIV-1 DNA PCR test at six weeks of age for all HIV-exposed infants not on ART.
If positive: Please fast track the infant for ART and continue CPT.
If negative: Please follow the 2013 PMTCT Clinical Guidelines Update for follow-up infant testing.

The infant needs Cotrimoxazole Prophylactic Treatment (CPT) from six weeks of age and routine vaccines.
For formula fed infants: Discontinue CPT if the 6-week PCR test is negative.
For breastfed infants: Discontinue CPT if HIV testing 6 weeks after the final breastfeed is negative.

	Weight	Daily Dosage
Cotrimoxazole (CTX) syrup (40/200mg/5ml) or tablet (80/400mg)	<5kg	2.5 ml
	5 - <14kg	5 ml or ½ tablet
	14kg - <30kg	10 ml or 1 tablet
	>30 kg	2 tablets

Please perform further infant HIV testing at 9 months, 18 months, if clinically indicated, and 6 weeks after the final breastfeed as per the 2013 PMTCT Clinical Guidelines Update.

Discharging Nurse/Dr: …… Sign: …… Date: ……/……/……

Follow-up date: ……/……/…… Site: ……