National consolidated guidelines for the prevention of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults

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National consolidated guidelines for the prevention of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults

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The Minister of Health, Dr. Aaron Motsoaledi announced changes in the ART guidelines during his budget speech in July 2014. These changes included changing the eligibility criteria for treatment from CD4 <350 to CD4 <500 as well as moving from WHO Option B to Option B+. These changes necessitated that the national guidelines be revised.

The Department of Health wishes to acknowledge the inputs of the large number of officials and experts that made inputs into these guidelines. Although these guidelines are based on the consolidated guidelines published by the World Health Organisation in 2013, the publication of these national guidelines would not have been possible without the inputs of our national experts.

ABBREVIATIONS AND ACRONYMS

3TC	Lamuvidine
AIDS	Acquired immune deficiency syndrome
ALT	Alanine transaminase
ANC	Antenatal care
ART	Antiretroviral therapy
ATV	Atazanavir
ARV	Antiretroviral
AZT	Zidovudine
BCG	Bacille Calmette Guerin (TB vaccine)
BD	Twice-daily
BMI	Body mass index
CD4	T-lymphocyte cell bearing CD4 receptor
CICT	Client-initiated counselling and testing
Cr	Creatinine
CrAg	Cryptococcal antigen
Cr Cl	Creatinine clearance
CSF	Cerebrospinal fluid
CTX	Cotrimoxazole
CLAT	Cryptococcal latex antigen test
CPT	Cotrimoxazole preventive therapy
d4T	Stavudine
DOT	Directly observed treatment
E	Ethambutol
EFV	Efavirenz
eGFR	Estimated glomerular filtration rate
ELISA	Enzyme-linked immunosorbent assay
EPTB	Extrapulmonary tuberculosis
EPI	Expanded programmme on immunisation
FBC	Full blood count
FDC	Fixed dose combination
FTC	Emtricitabine
GFR	Glomerular filtration rate
GIT	Gastrointestinal tract
Hb	Haemoglobin
HBcAg	Hepatitis B core antigen
HCT	HIV counselling and testing
HDL	High density lipoproteins
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
INH	Isoniazid
IPT	Isoniazid preventive therapy
IRIS	Immune reconstitution inflammatory syndrome
LDH	Lactose dehydrogenase
LFT	Liver function tests
LPV	Lopinavir
LPV/r	Lopinavir/Ritonavir
LTFU	Loss to follow-up
MCC	Medicines Control Council
MCH	Maternal and child health
MC&S	Microscopy, culture and sensitivity
MDR-TB	Multi-drug resistant tuberculosis
MNCH	Maternal, newborn and child health

MTCT	Mother-to-child transmission of HIV
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
NVP	Nevirapine
OD	Once daily
OHL	Oral hairy leukoplakia
OI	Opportunistic infection
p24	HIV antigen test
Pap smear	Papanicolaou test
PCR	Polymerase chain reaction (a laboratory nucleic acid detection test)
PHC	Primary healthcare
PI	Protease inhibitor
PICT	Provider-initiated counselling and testing
PMTCT	Prevention of mother-to-child transmission of HIV
PPD	Purified protein derivative (Screening test for TB)
PTB	Pulmonary tuberculosis
PLWHA	Person living with HIV/AIDS
QID	Four times daily
R (RIF)	Rifampicin
RBC	Red blood cells
RTH	Road to Health
S	Streptomycin
SANAC	South African National AIDS Council
Sd NVP	Single-dose nevirapine
SRH	Sexual and reproductive health
STI	Sexually transmitted infections
TMP-SMX	Trimethoprim/sulphamethoxazole – also known as cotrimoxazole
TB	Tuberculosis
TDF	Tenofovir
VL	Viral load (HIV)
WBC	White blood cells
WHO	World Health Organization
XDR-TB	Extensively drug resistant tuberculosis
PZA	Pyrazinamide

DEFINITION OF KEY TERMS

Term	Working definition in these guidelines
Adolescent	Aged 10 to 19 years inclusive
Early Adolescent	Age 10 to 15 years
Late Adolescent	Age 15 to 19 years inclusive
Adult	Older than 19 years of age
ART	Antiretroviral therapy refers to the use of combination of three or more ARV drugs to achieve viral suppression and is usually given for life
ARV	Antiretroviral drugs refer to the medicines themselves and not to their use
Child	10 years of ageand younger
CICT	Client initiated counselining and testing;Testing process initiated by an indivual who wants to learn his/her HIV status
Community health workers	Health workers who received standardised training outsidea nursing/medical curriculum
Continuum of care	Concept of an integrated system of care that guides and tracks clients over time, through a comprehensive array of health services spanning from screening for HIV, to diagnosis and management of HIV, to initation onto ART, retention in care and psychosocial support
Couple	Two people in an ongoing sexual relationship
Eligible for ART	Refers to people living with HIV for whom ART is indicated
Healthcare provider	Anyone who renders healthcare;includes doctors, nurses, counsellors
High-risk neonates	Neonates classified as having an increased risk of being infected with HIV in utero or at birth and are eligible for birth HIV PCR
HIV symptomatic infant	Any HIV-exposed infant displaying failure to thrive, haematological abnormality such as anaemia or thrombocytopenia, congenital pneumonia, pneumonia, hepatosplenomegaly, extensive oral candidiasis, significant lymphadenopathy and any opportunistic infections
HIV-exposed infant	Infant born to a woman who is HIV-positive or who becomes HIV-positive anytime during pregnancy, labor and delivery or breastfeeding. The infant is at risk of acquiring HIV infection from the mother and that the infant/child may test HIV-positive" on antibody testing, reflecting the mother's antibody
Infant	Child younger than one year of age
Key populations	Both vulnerable and most-at-risk populations
PICT	HIV testing and couselling recommended by healthcare provider in a clinical setting
Sero-discordance	Sexual partners where onepartner is living with HIV and the other is HIV-negative
Treatment failure	Treatment failure in adults and children, including infants, is defined by a persistently detectable viral load exceeding 1000 copies/ml (that is, 2 consecutive viral load measurements within a 2-month interval, with adherence support between measurements) after at least six months of using ARV drugs
Viral suppression	Refers to the aim of ART to maintain viral load below detectable levels of available assays (<50 copies/ml)
Virological failure	See treatment failure

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1 INTRODUCTION

1.1 BACKGROUND AND CONTEXT

The Governmentof South Africa has adopted a new outcome-based approach to accelerate the attainment of the objectives outlined in the Negotiated Service Delivery Agreement for the health sector. The main outputs include increasing life expectancy, reducing maternal and child mortality rates, combating HIV and AIDS, and decreasing the burden of diseases from TB, as well as strengthening health system effectiveness.

On 1 December 2009, on World AIDS Day, the Honourable President Jacob Zuma announced new key interventions to improve antiretroviral treatment (ART) access to special groups (all HIV-positive infants, and pregnant women and people with TB and HIV co-infection and with CD4 countsless than or equal to 350/µl), in order to decrease the disease burden, to address maternal and child mortality and to improve life expectancy. This resulted in more than 2,6 million people being initiated on ART by mid-2014.

In 2013, the fixed-dose combination pill (FDC) was introduced, made up of the regular three drugs used in the first-line regimen (TDF,FTC/3TC and EFV) to improve adherence and retention. On 23 July 2014, the Minister of Health, Dr. Aaron Motsoaledi announced that the threshold for initiation of ART will rise toCD4 count ≤500/µland that the PMTCT programme will now adopt the B+ approach, which entitles every pregnant and breastfeeding woman to lifelong ART regardless of CD4 count or clinical staging. This will be effected on January 2015.

Great strides have been made in the prevention of mother-to-child transmission (PMTCT) of HIV, with coverage of HIV testing of pregnant women now being close to 100%. PMTCT is offered in almost all health facilities in South Africa (98%), the percentage of HIV-positive pregnant women receiving ART to reduce MTCT has steadily increased from 83% in 2009 to 87.1% in 2012, and MTCT has decreased to 2.7% in 2011.

These successes are underpinned by a range of interrelated, evidence-guided strategic and operational plans, monitoring initiatives, and policies and guidelines – paving the way for South Africa to attain its objective of reducing mortality from HIV and TB.

There is a need, however, to strengthen focus on adolescents and prevent them from acquiring HIV and to treat and support them to take medication, in line with the new health department 2020 aspirational targets of having 90% of people tested for HIV and 90% of those eligible for treatment on treatment, with at least 90% of those on treatment virally suppressed. These new guidelines will assist in providing the necessary guidance towards improved management of HIV across different populations.

1.2 WHAT IS NEW IN THESE GUIDELINES

The main changes for pregnant/breastfeeding women, paediatrics, adolescents and adults are summarised in Boxes 1-3 below.

Box 1: Changes specific to pregnant/breastfeeding women

- Immediate initiation of lifelong ART for all HIV-positive women who are pregnant, breastfeeding or within 1 year post-partum, regardless of CD4 cell count
- Use of EFV as part of the first-line regimen, regardless of the gestation of the pregnancy
- Use of maternal lifelong ART throughout pregnancy and breastfeeding to reduce MTCT

- Viral load testing for women on ART ≥3 months at confirmation of pregnancy to direct management
- Repeat HIV testing for HIV-negative women 3-monthly during pregnancy, at labour/delivery, at the 6 week Expanded Programme on Immunisation (EPI) visit and 3-monthly throughout breastfeeding. This should be done during routine antenatal care, postnatal care and EPI/child health follow-up visits
- Women with contraindications to FDC should be considered high-risk pregnancies. They should be initiated on AZT immediately and referred urgently for initiation on to three single ART drugs
- Provision of birth HIV PCR for all neonates at high risk of HIV infection
- Use of extended 12 weeks NVP or dual post-exposure prophylaxis with NVP and AZT for infants where maternal viral load suppression may be inadequate

Box 2: Changes specific to infants and early adolescents

- Provision of ART for all children under 5 years, regardless of their CD4 cell count or clinical staging
- ART initiation for children ≥5 years now starts at CD4 count ≤500 cells/μl regardless of clinical staging
- Immediate initiation of infant ART with first positive HIV PCR, whilst waiting for confirmatory test results
- Use of second HIV PCR test as a confirmatory for positive HIVPCR test.
- No longer use viral load as part of baseline asessment for ART initiation in children

Box 3: Changes specific to late adolescents and adults

- Earlier initiation of ART at CD4 count ≤500 cells/μl
- Provision of ART for those with Hepatitis B (HBV) co-infection, regardless of CD4 count or clinical staging
- Harmonised ART regimen across populations, mainly pregnant and breastfeeding women, adolescents and adults
- Initiation of ART for all HIV/TB coinfected patients
- Inclusion of guidance on HIV for key populations
- Use of simplified fixed-dose combinations for ART
- Use of viral load for monitoring treatment success and early identification of treatment failure
- Routine cryptococcal infection screening for all HIV-infected patients with CD4 <100 cells/μl
- Use of Tuberculin Sensitivity Test (TST) as part of screening for IPT
- Use of third-line drugs for patients failing second-line regimens

1.3 RATIONALE FOR CONSOLIDATED GUIDELINES

- The consolidated, integrated guidelines offer guidance on using ARV drugs within the context of the continuum of HIV-related prevention, treatment and care. The major aspects of HIV-related care for all age groups and populations are addressed
- The respective ART guidelines for adolescents and adults have been combined with those for children and PMTCT, thereby harmonising ARV regimens and treatment approaches to the extent that is possible across different age groups and client populations
- Consolidation has allowed for new recommendations to be aligned across these groups, reduce duplication of information and promote consistency of approaches
- In addition, the consolidated document strengthens integration of services at facilities. This simplifies access to guidelines for healthcare providers for different groups of people seeking care. The guidelines reinforce family-centred care and one-stop-shop approaches to service provision

- The consolidated guidelines also enable more timely, consistent and simultaneous updates on new science and emerging practice applicable to all groups

1.4 GOALS AND OBJECTIVES

The main purpose of these guidelines is to improve the clinical outcomes of people living with HIV, reduce morbidity due to TB/HIV co-infection, reduce HIV incidence and avert AIDS-related deaths in the most cost-efficient manner by ensuring that people living with HIV start with the right therapy at the right time.

General objectives:

- Ensure timely HIV diagnosis, management, treatment and initiation of ARVs for treatment for all eligible populations to achieve best health outcomes in the most cost-efficient manner
- Contribute to strengthening of the health sector's capacity to deliver high-quality integrated health and wellness services
- Implement cascade management and ensure continuity of care
- Provide standardised and simplified less toxic treatment, which is harmonised amongst pregnant women, breastfeeding mothers, adolescents and adults in both the private and public sector
- Simplify guidance for health workers to improve the quality of HIV care for all people living with HIV and HIV-exposed infants
- Prevent new infections and reduce AIDS-related deaths among children, adolescents and adults

Specific objectives:

- Promote viral load testing as a preferred approach for monitoring ART success and diagnosing treatment failure
- Provide lifelong ART for all pregnant and breastfeeding women living with HIV
- Initiate ART earlier at a CD4 count threshold of 500 cells/µl
- Prioritise initiation of patients with CD4 count of $\leq$200 cells/µl, severe HIV disease and HIV/TB co-infection
- Strengthen retention in care and adherence to ART
- Reinforce phasing out of d4T in first-line regimens
- Ensure that HIV and TB services are provided as part of integrated maternal and child health, and sexual and reproductive health services
- Test all HIV-exposed and symptomatic children and initiate ART in all children under <5 years of age who are HIV-positive

1.5 TARGET AUDIENCE

All categories of healthcare professionals, healthcare workers, managers of the national health laboratory services, programme managers at district, provincial and national level and community-based organisations working with people living with HIV.

1.6 THE SCOPE AND CONTENT

These guidelines address clinical and programmatic aspects of HIV treatment and prevention amongst pregnant and breastfeeding women, children, adolescents and adults by making use of the continuum of care, from HIV testing and counselling, linkage with care and treatment, general HIV care and all aspects of ART management. This includes ART initiation (when to start and selection of ART regimenfor respective populations), adherence and retention strategies and monitoring and evaluation.

The guidelines do not provide detail for complementary programmes such as sexually transmitted infections, cervical cancer screening, contraception and fertility planning. These are covered in other guiding documents.

1.7 THE STRUCTURE AND CONTENT

The structure of these guidelines uses the continuum of care approach, also referred to as the treatment cascade, which reflects the different services that people living with HIV need to achieve optimal health outcomes. These include HIV testing and diagnosis, linkage to appropriate medical care (and other health services), support while in care, access to HIV treatment if eligible, support with treatment adherence and retention in care. The guidelines, however, do not include services for people who are HIV negative.

The document also looks at different population groups starting from pregnant and breastfeeding women, infants and children, adolescents and adults. Early adolescents are addressed in the same sections as children, while late adolescents are addressed in the adult sections.

Chapter 1: Describes the background, context, rationale and objectives of the guidelines and the target audience. It also provides a summary of what is new in these guidelines

Chapter 2: Outlines the guiding principles that underpin these guidelines

Chapter 3: Summarises HIV testing and counselling approaches and describes these in different populations

Chapter 4: Summarises general HIV care for individuals from the time that they are diagnosed with HIV infection to the time that they are initiated on ART. Addresses practices for linking people diagnosed with HIV infection to HIV care and treatment, the components of a general care package and preparing individuals for starting ART

Chapter 5: Outlines the principles of adherence to treatment and approaches for HIV disclosure

Chapter 6: Provides guidance of the eligibility criteria and optimal timing for ART initiation (when to start). Describes the first and second-line treatment regimen for the different populations (what to start or what to switch to) and provides recommendations for monitoring the response to and toxicity of ART. The chapter also includes guidance on labour, delivery and postnatal care for mother and baby

Chapter 7: Describes the different dosing recommendations for ARV drugs, ARV drug interaction with other drugs, their side-effects and toxicity

Chapter 8: Summarises the nutrition and feeding principles for infants and children

Chapter 9: Outlines the diagnosis and treatment of anaemia in people living with HIV for different populations

Chapter 10: Gives guidance on the prevention and management of opportunistic infections

Chapter 11: Provides guidance on a range of tools and indicators to be used to monitor the performance of programmes across the HIV continuum of care. It also provides data flow and reporting mechanisms for the different components of the treatment cascade

2 GUIDING PRINCIPLES

2.1 INCREASING EFFECTIVENESS AND EFFICIENCY OF PROGRAMMES

Due to the limited resources and competing priorities within a strained health system, it is essential to give priority to providing ARV drugs to people living with HIV who are eligible and most in need to achieve the desired impact.

2.2 MANAGING HIV AS A CHRONIC HEALTH CONDITION

With such a vigorous response to HIV, sustained high survival rates of patients can be expected and HIV-positive people now live longer, healthier lives, placing HIV in the realm of chronic diseases. The emerging chronic character of HIV means that the course of illness is longer and may also show some stability. As such, HIV interventions at primary healthcare settings should be re-conceptualised within the chronic disease management model which allows the coordination of interventions that occur at the level of clinical services, the community and individual patient.

2.3 STRENGTHENING INTEGRATION OF SERVICES

People living with HIV often have other health issues and integration of HIV services with primary healthcare (PHC), maternal, newborn and child health (MNCH) and TB provides an opportunity for more patient-centred care. Different services such as sexual and reproductive health, TB and HIV services, and operational programmes can be joined to maximise on collective outcomes.

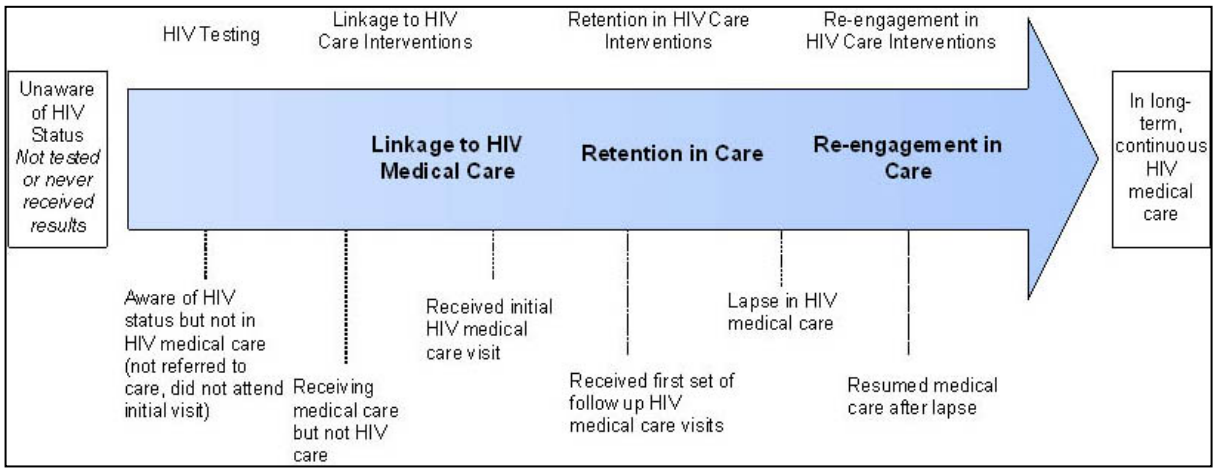
2.4 PROMOTING HUMAN RIGHTS AND HEALTH EQUITY

Access to HIV prevention, care and treatment is key to ensuring the universal right to care. Healthcare providers and institutions should render services based on principles of medical ethics and the right to equitable and quality healthcare. As signatories of the United Nations Convention of the Rights of the Child, healthcare providers in South Africa are obliged to comply with principles pertaining to children, which include the right of a child to life, survival and development; the right to equitable treatment and care and that all actions should be based on the best interests of the child.

2.5 PROMOTING A FAMILY APPROACH TO HIV CARE

Family-centred approaches represent the most appropriate and cost-effective models for responding to the challenges of HIV prevention, treatment and care. This includes ensuring that programmes provide appropriate care to women before, during and after pregnancy and, integrates maternal and child care services such that children have timely access to treatment and that early child development is supported. Couples and families, especially mothers and their infants, should receive healthcare at the same consultation regardless of the service point.

2.6 THE HIV CONTINUUM OF CARE APPROACH



This document gives guidance across the continuum of care, as shown in the diagram above, from HIV testing and counselling, through linkage with care and treatment, to general HIV care and retention in care. It also acknowledges the patient's cycle in and out of care and includes all aspects of ART.

HIV testing is the first component of the continuum of care approach and offers those that are unaware of their HIV status an opportunity to know their HIV status, or those who are HIV-negative to repeat the HIV test to be able to access appropriate care. This includes testing pregnant and breastfeeding women, early infant diagnosis using age-appropriate testing and testing adolescents as well as adults. Those who test negative should receive counselling to assess risk and be offered tailor-made risk reduction counselling that reinforces risk reduction behaviour.

3 HIV COUNSELLING AND TESTING

3.1 OVERARCHING PRINCIPLES OF HIV COUNSELING AND TESTING

HIV counselling and testing (HCT) is vital for identifying HIV-positive persons and provides an entry point to comprehensive HI prevention, treatment, care and support. It encourages individuals, couples, families and communities to know their HIV status and supports positive living, healthy lifestyles and good nutrition. It also helps identify and reduce behaviours that increase HIV transmission risks.

HCT is the first component of the continuum of care, and forms part of the HIV treatment cascade. For those who test HIV-positive, HCT provides an important opportunity for patient education on HIV disease and adherence, and is an essential step towards successful referral pathways that link patients to HIV care.

There are many different circumstances where a patient may be tested for HIV, for example; for individuals and couples; pregnant mothers for PMTCT as part of clinical care and screening; in cases of sexual assault or domestic violence; for abandoned babies; in response to a court order; and as part of medical male circumcision. In all instances, HCT must be ethical, confidential, based on human rights, conducted within a supportive environment, and be performed where there is relevant and adequate healthcare infrastructure.

All forms of HCT should be voluntary and adhere to the five C's: **consent, confidentiality, counselling, correct test results and connections to care, treatment and prevention services.** People who are tested for HIV after counselling must give informed consent to be tested and be informed of their right to decline testing.

HCT services are confidential, however, shared confidentiality with a partner or family members and trusted others and with healthcare providers is often beneficial and is usually encouraged.

There are two types of HCT, client-initiated counselling and testing (CICT), as well as provider-initiated counselling and testing (PICT).

Children may self-consent to HIV testing if they are 12 years of age and above, and the child is of sufficient maturity to understand the benefits, risks, and social implications of an HIV test. However, for children over the age of 12 with insufficient maturity to understand the benefits, risks, and social implications of a HIV test, a parent or caregiver must give consent for the test. The recognition of a caregiver as a surrogate decision-maker for children in relation to HIV testing recognises that the absence of a parent or guardian should not serve as a barrier to a child accessing HCT.A caregiver is defined as anyone who is responsible for the day-to-day care of the child in the absence of a parent or guardian.

These guidelines will discuss the general principles of HCT for pregnant and breastfeeding women, children and infants, adolescents and adults.

3.2 PROCESS FOR HIV COUNSELLING AND TESTING

All patients receiving both CICT and PICT should provide, at a minimum, verbal consent for HIV testing. Where possible, those receiving CICT can provide verbal consent only, which should be documented by the healthcare provider in the patient's file.

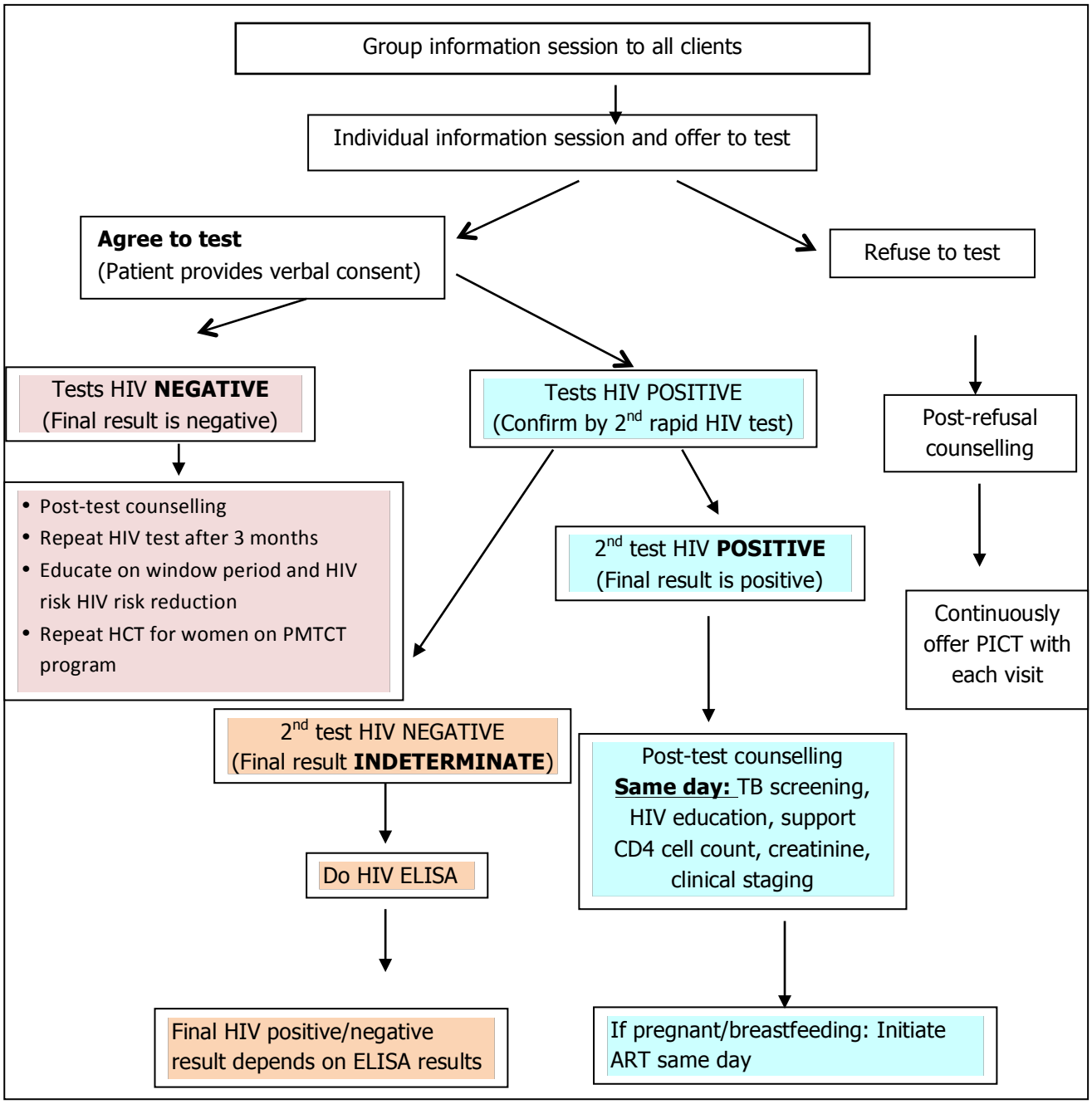
HCT should be done according to the Department of Health testing algorithm (Figure 1). All patients tested for HIV should be recorded in the HCT register, regardless of where the HCT is

done. Those who test positive for HIV should be further recorded in the pre-ART register to ensure tracking of linkage to care.

A group session should outline the benefits of HCT to the patient and if the patient is pregnant, it should include the benefits for the baby.

The individual HCT sessions should include an assessment of whether the information communicated in the group session has been understood and remaining questions answered, with an aim to clarify any misunderstanding, and address any concerns. For those who test HIV-positive, a second confirmatory HIV test is mandatory. All patients must receive post-test counselling, regardless of their HIV results. This includes risks for HIV transmission; safe sex and the use of condoms (even during pregnancy); contraception and fertility planning; HIV testing for sexual partners and children; repeat HIV testing for those who are HIV-negative; and PMTCT including safe infant feeding and infant prophylaxis.

Figure 1: Algorithm: HCT using rapid antibody test (adolescents/adults including pregnant/breastfeeding women)



3.3 MANAGING CLIENTS WHO TEST HIV-NEGATIVE

Patients who test HIV-negative should be offered a repeat test after 3 months if exposed, and educated on the window period. They should also be counselled on HIV risk reduction behaviour and be offered HIV prevention services such as medical male circumcision and condoms.

Pregnant and breastfeeding women who test negative should be considered part of the PMTCT programme and be offered routine repeat HIV testing throughout pregnancy, labour and breastfeeding periods. In South Africa, 4% of women who were initially HIV-negative become HIV-positive later in pregnancy. Regular repeat testing is essential.

3.4 SUMMARY OF WHEN TO REPEAT HCT

Table 1: When to repeat HCT

When to repeat HCT	
WHO	**WHEN**
Pregnant/Breastfeeding women (to detect HIV sero-conversion)	• Every 3 months throughout pregnancy • At labour/delivery • At the 6 week EPI visit • Every 3 months throughout breastfeeding (See Box 4)
General population	6– 12-monthly depending on risk
Adolescents	6– 12-monthly if sexually active or more frequently if they have new sexual partner/s or if not using barrier protection
If exposed to HIV (adult and adolescent)	After 6 – 12 weeks for window period
Key populations (MSM and sex workers)	Every 6– 12 months
Families of index cases	As soon as posible after the family member is diagnosed

3.5 HCT IN PREGNANT AND BREASTFEEDING WOMEN

- HCT should be offered to all pregnant and breastfeeding women with unknown HIV status or those who tested HIV-negative 3or more months previously
- All women attending antenatal care (both first-time attendees and women attending follow-up visits) should be given routine information about HIV testing and the PMTCT programme
- All pregnant women should be encouraged to book into antenatal care early, as soon as they believe they are or are confirmed to be pregnant. They should be offered HCT at their first antenatal visit, and if HIV-negative, follow HCT protocol as stipulated in section 3.6
- The partner/spouse and older children should be encouraged to test for HIV as well and they should be counselled on safer sex, provided with condoms and discuss future family planning options
- Regardless of whether they test positive or negative, all pregnant women should be considered as part of the PMTCT programme and should be offered information on the availability of PMTCT interventions during all healthcare consultations. They must also be counselled on safe infant feeding, be assisted in making appropriate feeding choices, be informed and counselled that exclusive breastfeeding for the first six months is the best option. They should also be informed and counselled that complementary foods should only be introduced from 6 months of age, with continued breastfeeding up to 12 months
- All pregnant women are encouraged to involve partners or spouses during HCT and in caring for the pregnancy. Condom use during pregnancy should be encouraged.
- All pregnant women are encouraged to be registered on MomConnect
- **Women who test HIV-positive** on the initial screening test should have their HIV status

confirmed using a second rapid HIV test with another test type in compliance with HCT policy as in Algorithm 1. Discordant results should be confirmed with an ELISA test. All confirmed HIV-positive women are eligible for immediate initiation with lifelong ART, preferably FDC

- **Women who initially test negative and subsequently test HIV-positive** at any time during pregnancy or breastfeeding should initiate FDC on the day of diagnosis following the guidance (refer to Section 6.1)
- **Women who choose not to be tested** must be provided with individual 'post-refusal' counselling and be offered HIV testing at every subsequent visit in a non-coercive manner during the antenatal period, at the onset of labour and, if this is not possible, shortly after childbirth. They should also be provided with a TB symptom screen at each visit
- **Unbooked women reporting in labour** must be counselled and tested for HIV at the earliest opportunity during labour and if positive, be provided with ART (refer to Section 6.1)

3.6 PREGNANT WOMEN WHO TEST HIV-NEGATIVE

All women who test negative should be offered repeat HIV testing every 3 months throughout pregnancy, at labour/delivery, at the 6-week EPI visit and 3 monthly throughout breastfeeding. They should also be provided with a TB symptom screen with each visit.

Post-test counselling of HIV-negative women should include:

- Education on HIV risk-reduction behaviour and where possible, must involve partners or spouses, focusing mainly on how to maintain their HIV-negative status
- Encourage correct and consistent use of condoms, particularly during pregnancy
- Provide routine antenatal, labour/delivery, postnatal and breastfeeding care
- Receive education and counselling about exclusive breastfeeding for the first 6 months, with complementary foods from 6 months
- If the woman remains HIV-negative, to continue breastfeeding up to 24 months

Box 4: Rationale for repeat HIV testing in HIV-negative women

In South Africa, approximately 4% of women who initially test HIV-negative in early pregnancy test HIV-positive later in the same pregnancy. Therefore, regular repeat testing is essential to detect new HIV infections (sero-conversions) occurring during pregnancy or breastfeeding.

HIV sero-conversion results in a very high viral load and subsequent high risk of MTCT. If new maternal HIV infection goes undetected, there is up to 30% risk of MTCT. Detecting new HIV infections quickly enables the woman to be started on ART as soon as possible and the infant to be identified and managed as HIV-exposed. Repeat testing also addresses false negative results. Always ensure the HIV test is conducted according to procedure, including waiting the correct duration of time before reading the result.

3.7 HIV COUNSELLING AND TESTING (HCT) IN INFANTS AND CHILDREN

3.7.1 HIV tests in infants and children (HIV PCR or Rapid HIV antibody test)

Table 2: Infants and children who should be offered HCT

RECOMMENDED INTERVALS FOR INFANT TESTING	
HIV PCR test	**Rapid HIV Antibody test**
At birth (targeted): Birth HIV PCR testing applies to all HIGH-RISK	**At 18 months:**

RECOMMENDED INTERVALS FOR INFANT TESTING	
infants including: • Low birth weight <2.5kg • Premature infants • Infants of mothers who were on TB treatment for active TB at any point during pregnancy • Infants born to mothers with VL>1000 copies/µl. • Infants of mothers who were on ART <4 weeks prior to delivery • Infants of mothers who were unbooked or diagnosed HIV-positive in labour or shortly after delivery • Breastfed infant of a newly diagnosed HIV-positive breastfeeding mother • Infants who are symptomatic at birth • These infants can be regarded as high-risk cases that need an urgent diagnosis so should receive HIV PCR as soon as possible after birth. • HIV PCR testing at 6 weeks should still be done on all HIV-exposed infants without confirmed HIV infection, regardless of earlier testing. • Any infant with a positive birth PCR should be urgently referred/discussed telephonically for ART initiation by a paediatric HIV expert **At 6 weeks:** • All HIV-exposed infants **At 16 weeks:** • All infants who received 12 weeks of NVP prophylaxis **Breastfed infants: (6 weeks post cessation of breastfeeding)** • All HIV-exposed infants – age appropriate: if <18 months old – do HIV PCR	• All HIV exposed infants **Breastfed infants: (6 weeks post cessation of breastfeeding)** All HIV exposed infants- age appropriate: if <18 months old- do HIV PCR **Family and social history (at all times)** • Parental request to test the child • Father or sibling with HIV infection • Death of mother, father or sibling • When the mother's HIV status is unknown, her whereabouts are unknown, or she is unavailable to be tested **All children (at all times) with:** • 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

3.7.2 What HIV tests to do in infants and children

HIV counselling and consent from parents or primary caregivers is required before testing young children. The two HIV tests that are available are:

- HIV antibody detection tests e.g. HIV ELISA test and rapid tests
- HIV viral detection tests e.g. HIV PCR (polymerase chain reaction) and 2nd HIV PCR for confirmation

HIV antibody detection tests cannot distinguish between the mother and the baby's antibodies. Maternal HIV antibodies are transferred via the placenta to the baby during pregnancy so that all vertically exposed babies will be born with HIV antibodies, and will test positive on antibody detection tests. These antibodies can remain in the baby's blood for up to 18 months. If antibodies to HIV are found in children <18 months of age, the child is HIV-exposed (i.e. born to an HIV-positive mother) and a viral detection test such as an HIV PCR is required to establish the infection status of the child.

The HIV DNA PCR test is highly accurate in determining the HIV infection status of an infant provided that all infants that test PCR positive have a confirmatory second HIV PCR test on the day of initiation of ART. The second HIV PCR to confirm every positive PCR test is **mandatory**. Initiation of ART should not be delayed while awaiting the result of the confirmatory viral detection assay. If the positive HIV status of a child already initiated on ART is disputed, additional HIV testing in consultation with the closest referral centre is warranted.

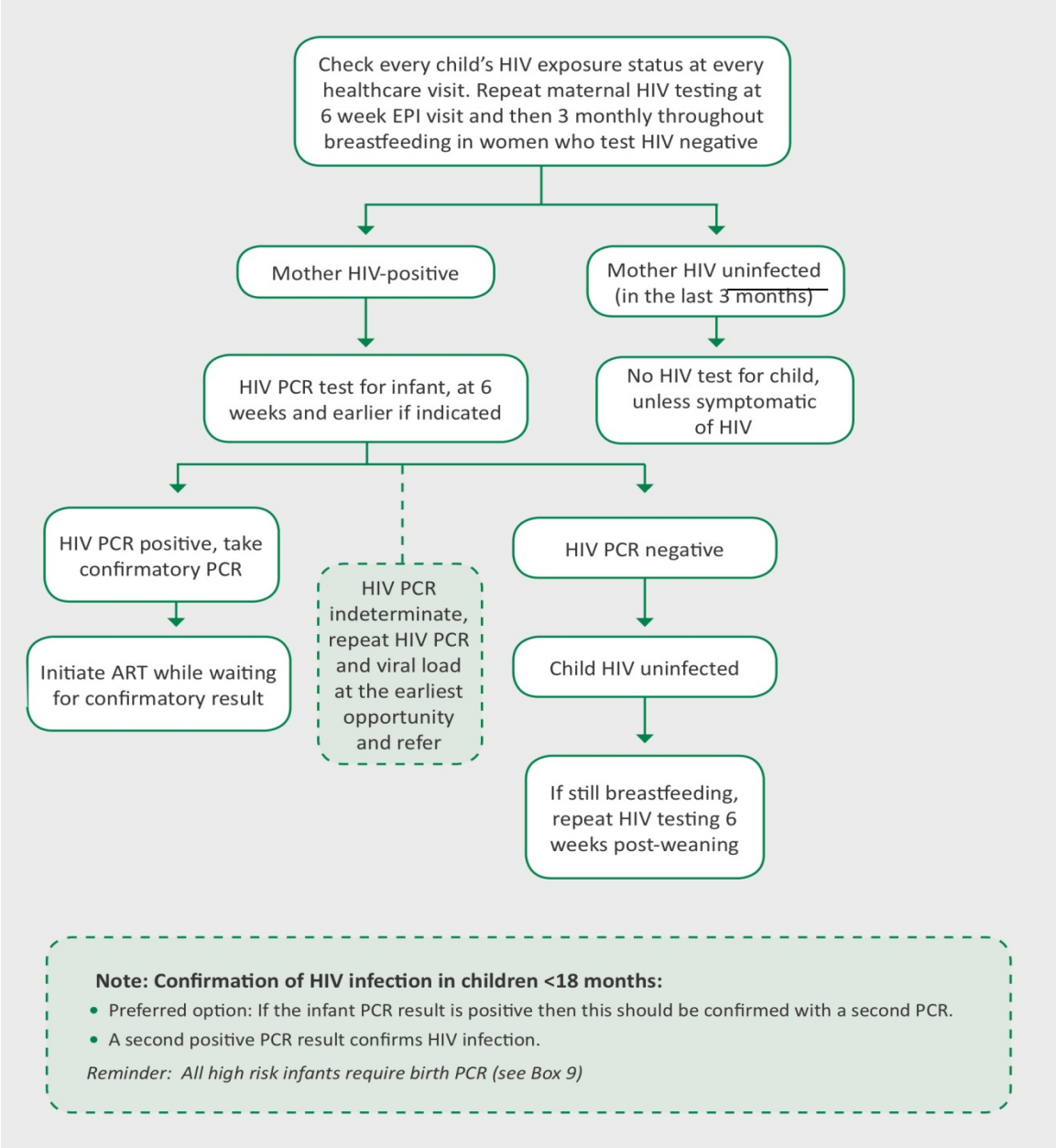
A negative antibody detection test at any age excludes HIV infection, provided the child was last breastfed 6 or more weeks before the test and has no clinical signs of HIV infection. If the mother is not available and there is no record of her HIV status, the HIV antibody tests can be done in children less than 18 months of age in order to determine whether or not the infant is HIV-exposed. If the rapid test is positive, immediately do an HIV PCR to determine if the infant is HIV-positive or HIV-negative.

Box 5: HIV PCR for infants <18 months

Under 18 months: Use HIVPCR

- This test detects HIV genes in human cells and is highly sensitive (98.8%) and specific (99.4%) at 6 weeks of age
- It will detect virtually all infections that have occurred in-utero, during labour, delivery and breastfeeding in infants younger than 18 months. An HIV-exposed but uninfected child will test PCR negative and an HIV-exposed infected child will test PCR positive
- However, there is a possibility of a false negative or indeterminate result, particularly at the 6 week PCR test because the infant has been on NVP prophylaxis. If an infant has experienced MTCT but is on NVP prophylaxis, then the 6-week PCR may be negative or indeterminate. It is essential that any infant who presents to a facility with symptoms of ill health has a HIV PCR repeated, even if the 6 week PCR is negative
- The HIV PCR test is highly accurate in determining the HIV infection status of an infant provided that all infants that test PCR positive have a confirmatory second HIVPCR test as stipulated in the algorithm in figure 2 on the day of initiation of ART
- Initiation of ART should not be delayed while awaiting the result of the confirmatory HIV PCR test
- If the positive HIV status of a child already initiated on ART is disputed, additional HIV testing in consultation with the closest referral centre is warranted
- Establish the best methods for reliably obtaining PCR test results from the laboratory and ensure effective troubleshooting if PCR test results are problematic

Figure 2: Algorithm for testing children <18 months of age



HIV-exposed infants who are PCR negative 6 weeks after stopping breastfeeding should have a confirmatory rapid test at 18 months of age. Infants of newly diagnosed HIV-positive breastfeeding mothers must receive an age appropriate HIV test; HIV PCR if <18 months and HIV rapid test if ≥18 months, and start on NVP and AZT immediately. If the HIV test is negative, stop the AZT and continue daily NVP for 12 weeks. If the infant's HIV test is positive, stop NVP and urgently initiate paediatric triple ART while retesting and confirming the HIV result.

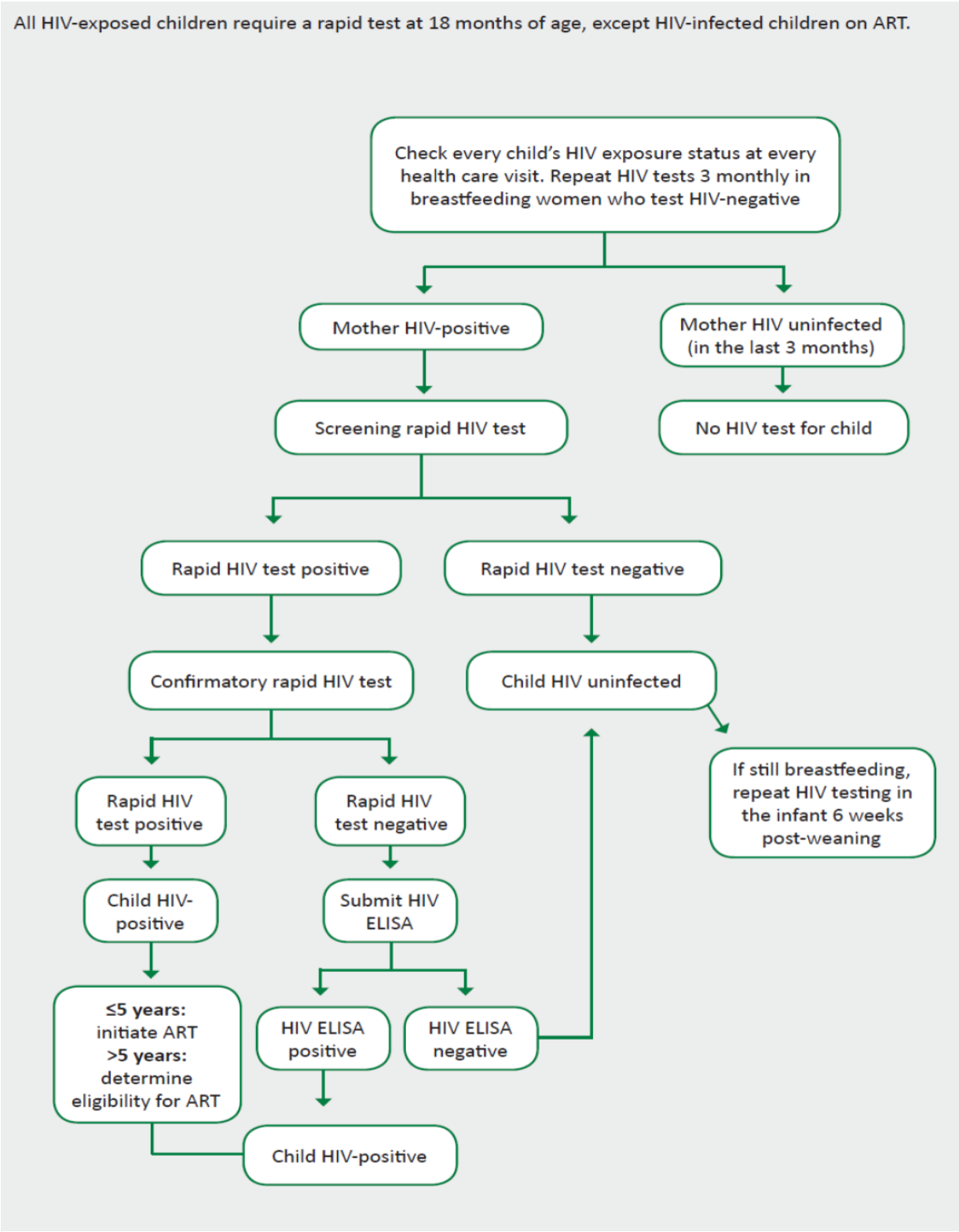
Box 6: HIV rapid antibody test for infants ≥18 months

Older than 18 months: Use rapid HIV antibody test

- Use the same test used to diagnose or exclude HIV infection in adults
- If negative, the child is not infected provided there are no clinical features of HIV and breastfeeding stopped >6 weeks before the HIV test was done
- If positive, a second, different rapid test is used for confirmation. If the second rapid test is positive, the child is infected

- If the second rapid test is negative, an HIV ELISA test should be submitted to establish the child's HIV status
- All HIV tests performed and results obtained must be documented in the Road-to-Health (RTH) booklet, including the laboratory tracking barcode

Figure 3: Algorithm for routine testing children ≥18 months of age



Note: Healthcare workers must check with every child >18 months whether they were HIV exposed. If yes, whether they received this 18 month test. If the 18 month test was missed, do an HIV rapid test regardless of how much older than 18 months the child is.

Box 7: HIV PCR for infants, including abandoned infants

- HIV rapid antibody tests can be used in children less than 18 months of age in order to determine whether or not the infant is HIV-exposed
- The HIV status of abandoned infants less than 72 hours old should be established as soon as possible
- If the rapid test is positive, the child should be given stat dose and daily Nevirapine (NVP) until six weeks of age
- If the rapid test result cannot be obtained within 1-2 hours, treatment with NVP should be commenced
- If the infant tests antibody negative, NVP should be discontinued.
- The child should receive other treatments such as Cotrimoxazole (at 6 weeks) for HIV-exposed infants if the status is still unknown or the infant is HIV-positive
- HIV PCR should be done if the rapid test is positive. If HIV PCR is positive, infant ART should be initiated urgently

3.7.3 Repeat HIV testing follow-up for HIV-exposed infants

Early infant diagnosis is vitally important and is closely linked to well-baby care. In the first year of life, monthly visits that incorporate EPI should be scheduled for all infants during which routine health checks should be performed. Every contact with the healthcare service should be used to ensure that the child's HIV-exposure status is known and documented in the RTH booklet. The HIV-exposure status of the child can be established by referring to the RTH booklet, taking a history from the mother or offering the mother an HIV test if her status is unknown or she requires repeat testing (Figure 1).

Table 3 provides the recommended routine immunisation schedule for all babies; HIV-exposed, HIV-positive and non HIV-exposed infants.

Table 3: Expanded Programme on Immunisation (EPI) schedule

Age	Immunisation	
Birth	• BCG • OPV 0	• Bacillus Calmette-Guérin (Do not give BCG at birth if the mother had TB) • Oral Polio Vaccine
6 Weeks	• OPV1 • RV 1 • DTaP-IPV-Hib • Hep B1 • PCV1	• • Rotavirus Vaccine • Diphtheria, Tetanus, acellular Pertussis, Inactivated Polio Vaccine and Haemophilus influenza type b • Hepatitis B Vaccine • Pneumococcal Conjugated Vaccine
10 weeks	• DTaP-IPV-Hib-Hep B2	Diphtheria, Tetanus, acellular Pertussis, Inactivated Polio Vaccine and Haemophilus influenza type b
14 weeks	• RV2 • DTaP-IPV-Hib • Hep B3	

Age	Immunisation	
	• PCV2	
6 months	• Measles vaccine	Only for HIV-positive children
9 Months	• Measles Vaccine 1 • PCV3	
18 Months	• DTaP-IPV-Hib • HepB4 • Measles Vaccine 2	
6 years	Td Vaccine	Tetanus and reduced strength Diphtheria Vaccine
9 years	HPV	
12 Years	Td Vaccine	

3.7.4 Using monthly well-baby visits for HCT

HIV testing at 6-week immunisation visit

- Cotrimoxazole prophylaxis for all HIV-exposed infants starts at 6 weeks of age
- At 6 weeks of age, establish and document every infant's HIV exposure status. PCR testing should be performed in all HIV-exposed infants at 6 weeks of age, including HIV-exposed infants with a negative PCR performed at birth. Consent to test the child for HIV can be obtained from the primary caregiver
- Appropriate responses are based on the mother's HIV status is shown in Table 4 below
  - Maternal adherence should be reinforced
  - Infant HIV PCR testing should be conducted
  - Initiate infant onto Cotrimoxazole syrup from 4-6 weeks after birth
  - Discontinue NVP syrup unless infant is eligible for extended (12 week) course (indicated in Table 9)
  - Obtain results for HIV PCR within the week. If positive, take a second HIV PCR and initiate ART while waiting for the confirmatory result. Continue Cotrimoxazole syrup
  - If the HIV PCR test result is negative, continue Cotrimoxazole syrup until the infant is confirmed HIV uninfected and is *fully weaned*
  - Repeat infant HIV PCR 6 weeks after breastfeeding cessation
  - Monitor infant growth
  - HIV-negative mothers should be offered an HIV test; if the result is positive, the infant should have an HIV PCR test
  - All mothers should be counselled about options for contraception
  - Reinforce infant feeding counselling

Table 4: HIV testing at six-week visit

Mother's HIV status	Action
Positive maternal HIV status	All infants born to HIV-positive women require an HIV PCR
Negative maternal HIV status	Rapid test should be offered to mother to ensure she has remained HIV-uninfected
Unknown maternal HIV status	Offer a rapid test to the mother. If she tests positive then her infant should have a HIV PCR at the same visit. Provide the mother with the care she requires

Mother's HIV status	Action
Unknown maternal HIV status and mother refuses testing	Post-refusal counselling with encouragement to test at the next visit or at any time. If infant shows any signs suggestive of HIV then advise mother on the necessity to test the infant even if she refuses testing for herself

HIV testing at 10-week immunisation visit

- This is the next well-baby visit at which the HIV PCR result should be available
- If the HIV PCR result is available sooner and is positive, contact the mother or caregiver and arrange for an earlier visit as the highest risk of infant death is between 2 and 3 months of age
- If no HIV PCR results are available and a repeat sample is required, arrange for an earlier visit
- Ensure that systems are in place to trace HIV PCR results and infants who have defaults in their visits
- Ensure that it is possible to fast-track positive HIV PCR results to mother-infant pairs
- If the HIV PCR is positive, a confirmatory HIV PCR must be sent immediately and the infant should be initiated onto lifelong ART (do not wait for the confirmatory result before initiating ART)
- If the HIV PCR test is negative and the child has not been breastfed since birth, then the infant is not infected
- If the HIV PCR test is negative, but the child was breastfed (within the six weeks preceding the test) or has continued to be breastfed, then repeat HIV testing will be required 6 weeks after breastfeeding has stopped or anytime if the child develops clinical features suggestive of HIV infection. The repeat HIV test will be a PCR if the child is below 18 months of age and an antibody rapid test if the child is older
- If the 6 week HIV PCR result is negative but the infant is symptomatic of HIV at the 10 week follow-up visit then repeat the HIV PCR test

HIV testing at monthly well-baby visits between 10 weeks and 18 months

- Every child's HIV-exposure status should be determined at each monthly visit and mothers of unknown status or previously negative HIV status should be offered HIV testing according to Figure 1 (Algorithm 1, Section 3.2)
- Check at every visit if breastfeeding has stopped to ensure that an age-appropriate HIV test is performed 6 weeks after weaning
- HIV testing should be repeated at any point if the child is symptomatic

HIV testing at 18-month immunisation visit

- Remember all HIV-exposed children with a negative HIV PCR test should have a repeat HIV (antibody) test at 18 months of age. Final infection status should be documented in the RTH booklet
- An HIV (antibody) test at 18 months of an HIV-positive child on ART is not required
- Children still breastfeeding at the 18-month visit require a further HIV antibody test 6 weeks after weaning has occurred

3.7.5 HIV testing for breastfed children

Postnatal transmission via breast milk can occur at any time during breastfeeding. If breastfed infants test HIV PCR positive at any age then they are confirmed HIV-positive. They should be initiated on ART, a confirmatory HIV test sent and breastfeeding should be continued. HIV infection can only be excluded by documenting a negative HIV test 6 weeks after breastfeeding has

completely stopped. Depending on the age of the child, a viral detection or antibody detection test to assess for postnatal transmission of HIV should only be done 6 weeks after breastfeeding has stopped.

All breastfed, HIV-exposed children should receive an HIV test as follows:

- HIV PCR test at 6 weeks of age
- Repeat HIV PCR at 16 weeks for all infants who received an extended course of 12 weeks of NVP prophylaxis
- A rapid HIV test at 18 months of age
- An age-appropriate HIV test 6 weeks after breastfeeding has stopped
- Additional age-appropriate HIV tests if an HIV-uninfected, breastfed infant develops clinical features suggestive of HIV or if the mother is considering weaning, and her decision will be influenced by the child's HIV status

3.8 HCT IN ADOLESCENTS

The population of South African children with HIV are ageing into adolescence as a result of a maturing HIV epidemic, with an increase in the number of long-term non-progressors. The country has seen improved survival of HIV-positive children due to the provision of ART and an increase in behaviourally HIV-infected adolescents. Addressing the specific needs of perinatally HIV-infected adolescents and behaviourally HIV-infected adolescents and preventing pregnancies and HIV in adolescents are national priorities.

Even though adolescence is marked by rapid physical, intellectual and emotional growth, there is significant variation in the timing of developmental milestones and in the timing and degree of changes in rates of growth during adolescence. This means that there can be variation in development among adolescents of the same age, and that there are often significant differences between girls and boys.

For many reasons, adolescents are less likely than adults to be tested for HIV and less likely to be linked to services, whether they test positive or negative. More perinatally HIV-infected children are surviving into adolescence. Adolescents are vulnerable to and at relatively high risk of HIV infection.

HCT is not an end in itself, but rather a means to engage adolescents and link them to essential HIV treatment, care and prevention interventions. It also provides an opportunity to encourage health-seeking behaviour both among those testing negative (e.g. future re-testing for HIV, safe sex etc.) and those testing positive (e.g. linking to care services and supporting adherence to ART).

The following groups of adolescents are considered to be **most-at-risk for HIV** (often referred to as adolescents from key populations):

- Adolescent males who have sex with men (MSM)
- Adolescents who are sexually exploited and adolescents engaged in sex work
- Adolescents who inject drugs
- Transgender (TG) adolescents (male and female)
- Adolescents affected by AIDS (orphans and children of chronically ill caregivers)
- Adolescent clients of sex workers and the partners of these clients

It should also be noted that women aged 15 to 24 are the group with the highest rate of new HIV infections in South Africa and should therefore be considered to be at most risk.

HCT, with linkages to prevention, treatment and care should be offered to these adolescents. They should be counselled about the potential benefits and risks of disclosure of their HIV status to others and empowered and supported to determine if, when, how and to whom to disclose. Regardless of the HIV acquisition route, under-utilisation of HCT services results in late diagnosis and increased uptake results in earlier diagnosis and more effective care.

Disclosure of HIV status is a continuous process that occurs throughout adolescence and ranges from informing young people of their HIV status – either at diagnosis or later, depending upon their age – to adolescents independently sharing their HIV status with others when they are ready to do so. Adolescents and young people need a lot of support from healthcare providers, peers and the community to disclose safely and confidently, and to be able to cope with any negative reactions from family, friends and their community. Adolescents and young people in key populations are particularly sensitive to confidentiality issues as they often risk legal consequences and abuse linked to their high-risk practices and lifestyles.

3.9 HCT IN ADULTS

All adults should be offered HCT whenever an opportunity arises, and this should be repeated annually, depending on the risk. HCT for couples is voluntary. Where possible, it should be encouraged so as to identify sero-discordant couples and link the HIV-positive partner to treatment and support and to educate the HIV-negative partner about risk reduction. Couple HCT increases access to earlier ART initiation and reaches more men. This can be extended to family counselling to identify children and adolescents in households who were not previously diagnosed.

4 LINKAGES AND RETENTION IN CARE

4.1 GENERAL PRINCIPLES FOR LINKAGES AND RETENTION IN CARE

The outcome of HCT is only successful if those who are HIV-negative are supported to reduce their risk of acquiring HIV, and if those who are HIV-positive are successfully linked to the continuum of HIV care. For various reasons there is significant loss of patients from the time that people are diagnosed with HIV to the first assessment of ART eligibility. The treatment cascade shows two main leakages; people lost between a positive HIV test and the CD4 test, and those lost between CD4test and the return visit for the CD4 test result.

Barriers include having to travel long distances to the clinic, long waiting times at the clinic, clinic staff shortages, inability to take time off work, lack of full understanding of the treatment plan, and fear of stigma and discrimination. However, when effectively linked to prevention, treatment and care services, HCT enables those being tested to make positive health-related decisions.

It is the responsibility of healthcare providers to identify appropriate services, connect with referral services, and clearly outline pathways of linkage and support patients, especially adolescents, to engage with the services that are available. People living with HIV need to enrol in care as soon as they become aware of their HIV-positive status.

Box 8: Strategies to improve linkage to care

- Post-test counselling provides an opportunity to discuss the importance of linking to other HIV-related services and sets out referral pathways with the patient. It is imperative that post-test counselling is provided to all clients, whether their results are HIV-positive or HIV-negative
- If acceptable to the adolescent, allow and encourage them to invite a supportive adult or friend to be present to support them
- At the time of HIV diagnosis, the healthcare provider should involve the patient in the decision-making process of ART initiation, and explain the entire treatment plan and follow-up visit schedules
- During HCT, identify and address any possible barriers to linkage to care
- Assessment for ART eligibility should be timely and done within clear referral pathways
- Services should be provided within the same facility where possible and minimise sending patients to a different institution for ART eligibility
- In terms of referrals, directly make appointments with the receiving institution on behalf of the patient and provide the patient with the appointment date and a referral letter
- Provide the patient with the contact information for referral services
- Treat mother and baby as a pair and provide services to both
- Where possible, engage patient in post-diagnosis support groups
- Register pregnant women on MomConnect on the first antenatal care (ANC) visit
- Use of SMS technology to remind patients of appointments
- Capacity-building and support for peer support worker approaches and community-based outreach workers
- Encourage the buddy system, whereby mutual support is provided by someone in a similar situation, or with a similar experience
- Loss to follow-up protocols to keep track of adolescents through the system
- Make a list of people close to the adolescent who could assist the adolescent to adhere to treatment and attend appointments

4.2 THE WELLNESS PROGRAMME (PRE-ART)

When patients have been diagnosed with HIV but are not yet eligible for ART initiation, they should be kept within the wellness programme where they are encouraged and given support to live a healthy lifestyle. Their CD4 cell count should be checked regularly, at least 6-monthly to assess eligibility for ART. The pre-ART or wellness programme should include the following:

- TB screening and clinical staging with every visit and initiate INH prophylaxis (IPT) if eligible
- Screening and management of sexually transmitted infections
- Information and counselling on how to avoid HIV transmission to sexual partners and children
- Information and counselling on risk-reduction and combination HIV prevention approaches
- Support for disclosure and partner notification
- Information and counselling related to fertility, including planning for conception or contraception, as needed
- Counselling on nutrition and healthy lifestyle
- Screening and management of co-morbidities and non-communicable diseases
- Repeat CD4 testing and WHO clinical staging 6-monthly in adults and adolescents
- An annual cervical cancer screening (pap smear) for all HIV-positive women
- Advise patients to come back whenever they have health problems

4.3 PREPARATION FOR INITIATION ON ART

It is important to discuss the patient's willingness and readiness to start ART. They should be educated on the benefits of treatment and the possible side-effects. Consider the nutritional status of the patient, co-morbidities and possible drug-interactions, and address any mental health and substance abuse issues.

Where children are concerned, a caregiver who will be responsible for ensuring that the child takes treatment and adheres to clinic appointments should be identified. A comprehensive nutritional, growth and development assessment for children and adolescents is essential.

Risk reduction counselling and combination HIV prevention approaches should be emphasised including safe sex, availability and use of condoms (especially during pregnancy), contraception and future fertility.

4.4 PREPARATION OF PREGNANT HIV-POSITIVE WOMEN

- HIV-positive pregnant women should be offered information on the availability of PMTCT interventions at all healthcare consultations and not only when visiting the antenatal clinic
- At the first ANC visit/HIV diagnosis, the patient should have a CD4 cell count test and serum creatinine taken and be staged clinically
- The patient should have a TB symptom screen at each visit, with further TB investigations if any of the answers to the screening questions are positive
- Patients should be screened and swiftly treated for syphilis and other STIs, in line with basic antenatal care
- The patient should receive FDC at the first antenatal visit, whether newly diagnosed or known to be living with HIV but not on ART. If FDC is contraindicated, these patients are considered to have high-risk pregnancies and require urgent referral to HIV/ART services. They should be given AZT 300mg twice daily until triple ART can be initiated
- HIV-positive women should return 1 week after their initial ANC visit to follow up their creatinine and CD4 cell count result and be managed accordingly
- Patients should receive counselling on safer sex, family planning, postnatal contraception, partner testing and routine cervical cancer screening
- Patients should undergo nutritional assessment and equipped with appropriate nutritional

care and support

5 ADHERENCE, PSYCHOSOCIAL CARE AND SUPPORT

5.1 PRINCIPLES OF ADHERENCE TO HIV TREATMENT

Education on adherence to treatment starts at the beginning of the treatment cascade, when a patient is diagnosed as HIV-positive. Adherence includes taking treatment as prescribed, keeping to appointments for test results, referrals and further investigation. The patient's motivation to continue engaging with care regardless of eligibility for ART is influenced by their experience with the healthcare system and the attitude of healthcare providers.

Patients who are supported in their adherence efforts are much more likely to maintain viral loads (VL) that are undetectable. The link between VL suppression, clinical outcome and adherence should be explained. This should clarify to the patient how the VL is used to show that the treatment is working and allow patients to identify obstacles to successful adherence.

Adherence, especially to lifelong treatment, requires ongoing assessment and monitoring, which should be part of each clinic visit, as factors that influence adherence are dynamic and require different approaches as they change over time.

- Adherence counselling should start at the time of diagnosis, where patient education on HIV should be explained in detail. The treatment plan should be explained and expected clinic visits discussed
- Encourage disclosure to family or friends who can support the treatment plan
- Monitor and offer ongoing adherence support. Be supportive and non-judgmental to encourage open and honest patient communication
- Adherence goal is >95% of doses taken. Patients with adherence <80% require more adherence support
- Missed appointments for prescription pick-ups are a powerful predictor of poor adherence, and should trigger immediate questions about issues that may affect attendance and adherence
- Routine adherence discussion/education with adherence counsellors is valuable. This should be an open-ended discussion, with time for questions and key points about adherence reinforced
- Patients should be reassured on the transient nature of side-effects such as nausea and vomiting at treatment initiation
- Address adverse events, interim illness and issues around stigma and disclosure
- Encourage caregiver participation in a support group
- There should be monthly counselling visits for the first 3 months and quarterly thereafter, and feedback given to the rest of team to develop a better profile of the patient's environment
- Identify food insecurity and actively address this through government support programmes
- Ensure communication between clinic visits and between referral points

5.2 STRATEGIES TO PROMOTE ADHERENCE

Box 9: Strategies to promote adherence

Ensure quality adherence counseling	**Support patient with adherence tools**
• Spend time with the patient and explain thedisease, the goals of therapy and need for adherence • Discuss the role of VL and suppression	• Encourage attendance and participation in asupport group • Self reporting on adherence should beencouraged

• Negotiate a treatment plan that the patient can understand and commits to • Explain to patients how to avoid adverse drug-drug interactions • The patient should understand the possible consequences of mixing other prescribed or recreational drugs and subtances	• Reinforce use of pillboxes or a daily dosing diary • Encourage a 'treatment buddy' • Caregiver and/or patient are introduced to therapeutic counsellor and patient advocate, if available and agreed to or nominated by patient, and home visit is arranged
Impart knowledge • *Improve understanding*: patients often have limited knowledge and understanding about why they have to take ART, how it works and how it benefits them • Focus on patient-provider shared decision-making • Involve patient's family/caregiver if possible • Advise on how to cope with medication costs • Provide prescription instructions clearly • Reinforce all discussions often • Provide pre-treatment information and education as per visit schedule	**Modify patient behaviour** • Empower patients to manage theircondition themselves • Ensure patients understand the risks of nottaking their medications • Address fears and concerns • Provide encouragement and recognition for adherence

5.3 HIV DISCLOSURE IN CHILDREN, ADOLESCENTS AND ADULTS

All patients should be supported for disclosure and partner notification. The United Nations Convention on the Rights of Children (Article 12) states that children have the right to participate in decisions about their own healthcare. The decision to inform the child of his/her HIV status should be viewed as mandatory and be age appropriate. It is important that disclosure follows a planned process and to understand that there are levels of disclosure over time. The process of disclosure is cyclical, it needs to be repeated as new information or deeper levels of information are shared with the child.

Diagram 1: Approaches to HIV disclosure in children

Box 10: HIV disclosure in children

Reasons for disclosing HIV status in children	**How to communicate with children**
• As the age of children living with HIV steadily increases, it will result in a population of sexually active young people with HIV infection • Keeping their HIV-positive status a secret can be a burden • Disclosure should always be in the best interests of the child. This applies to the disclosure itself as well as the manner of disclosure • Benefits of disclosure include recognition of the child's autonomy, increased intimacy with those close to the child and improved psychological adjustment • Children may need to prepare for tasks ahead (sickness, painful procedures etc.) • Children often know more than adults give them credit for • Children who are not told about their disease often have much more anxiety and distress • Disclosure needs to take place before the stage of adolescence	• Find out how much the child knows about his/her illness and what they want to know • Children need to know that they are loved and will be cared for • Assure the child that his/her HIV status or the parent's HIV status is not a punishment for any wrongdoing • Educate them on how HIV is transmitted • Disclosure must be age appropriate • Be honest. If you don't know the answer to the child's questions, say so • Be led by the child in terms of the amount of information he/she requires • Use age-appropriate language in line with education and emotional readiness • Anticipate possible responses by the child and plan for the future • Anticipate the impact of the disclosure on other family members, friends, the school and the community and plan for this • Monitor the child's behaviour after disclosure (sleeping, school problems, and withdrawal). Changes in behaviour can indicate a need for more support and intervention • Be respectful of the child's needs, feelings and responses

5.4 STEP-UP ADHERENCE IN PATIENTS WITH NON-ADHERENCE OR TREATMENT FAILURE

Box 11: Strategies for stepping-up adherence

This applies to all patients with <80% adherence at any visit and those with first VL>1000 copies/ml

- The therapeutic counsellor/nurse or doctor needs to re-educate the patient, caregiver and their 'buddy' about the importance of adherence
- The long-term benefits of adherence need to be re-emphasised
- Evaluate the support structures in place; whether they are appropriate, how they can be improved and explore other options
- Encourage the patient to consider the use of pillboxes and/or a daily dosing diary
- Encourage the patient to participate in a support group or create a link with a patient advocate
- Consider doing a psychological profile, assess for mental health issues/substance misuse
- Investigate the family situation through a social worker and actively address food security
- Increase home visits by therapeutic counsellors/patient advocates to daily or weekly at a minimum
- Spot pill counts can be done at home

6 ANTIRETROVIRAL THERAPY

The goal of ART treatment is to reduce the patient's VL to an undetectable level and ensure that it remains undetectable, as well as to improve the immunological status with the CD4 count rising and remaining above the baseline.

6.1 ART IN PREGNANT AND BREASTFEEDING WOMEN

All HIV-positive women require management and care during the antenatal, labour, delivery and postnatal phases. This includes iron, folate and calcium supplementation; haemoglobin testing; the provision of ARVs; the diagnosis, prevention and management of opportunistic infections, including TB; the modification of obstetric practices, especially during labour and delivery; and counselling on infant feeding, safer sex, family planning and contraception.

Women who are put on a FDC (TDF+FTC+EFV) in their pregnancy should be monitored and managed, where possible, by the same provider in the same facility through the antenatal and postnatal periods until the end of breastfeeding. **They should then be referred to appropriate services to continue lifelong ART as part of the general adult ART population.**

6.1.1 When to start: eligibility criteria for ART in pregnant and breastfeeding women

It is important to avoid unnecessary delays in initiating ARVs during pregnancy or breastfeeding. All HIV-positive pregnant women should receive ART with appropriate counselling from their first antenatal visit regardless of gestational age. The first choice ART regimen is TDF+FTC+EFV given as a FDC. All women should start this regimen at the first antenatal clinic visit. Baseline CD4 cell count should also be done to assess eligibility for CrAg and CTX, but should not delay ART initiation.

All HIV-positive pregnant women are eligible for lifelong ART. They should receive adequate support and counselling, particularly addressing ART adherence, and should be retained in ART services throughout pregnancy, breastfeeding and as part of lifelong care.

All women diagnosed as HIV-positive within the first year postpartum are to be initiated on lifelong ART regardless of CD4 count or infant feeding practice.

Table 5: Eligibility criteria for pregnant and breastfeeding women

POPULATION	WHEN TO START	COMMENTS
Pregnant and breastfeeding women	Initiate lifelong ART in all pregnant or breastfeeding women on the same day of diagnosis regardless of CD4 count	Emphasise exclusive breastfeeding for the first 6 months, with complementary feeding only from 6 months and breastfeeding continued until 12 months
	All unbooked women who test positive during labour should be given prophylactic ART during labour and initiated on lifelong ART before being discharged	

6.1.2 What to start: First-line ART regimens in pregnant and breastfeeding women

Table 6: ART regimens for pregnant and breastfeeding women

FIRST-LINE ART REGIMENS		
Population	**Drugs**	**Comments**
1st ANC visit		
All pregnant women not on ART (any gestational age) All breastfeeding women not on ART	TDF + 3TC (or FTC) + EFV Provide as fixed-dose combination (FDC)	If there is a contraindication to the FDC (Contraindication to TDF: renal insufficiency Contraindication to EFV: active psychiatric illness): start AZT immediately and refer to Boxes 2 and 3
Pregnant women currently on ART	Continue current ART regimen Change to FDC if on individual first-line drugs and virally suppressed and no contraindications to FDC	Check a VL as soon as pregnancy diagnosed, regardless of when the last VL was done Patients with confirmed 2nd or 3rd line regimen failure should not breastfeed their infants
2nd ANC visit (1 week later)		
Pregnant women Creatinine ≤85µmol/l and any CD4 cell count	Continue FDC	
Creatinine >85 µmol/l TDF contraindicated	Stop FDC, initiate AZT if Hb ≥7g/dl	High-risk pregnancy: refer urgently for alternate triple therapy within 2 weeks, with dose adjustment if indicated, and investigation of renal dysfunction
Contraindication to EFV (active psychiatric illness)	Continue AZT until initiated on individual drugs TDF+3TC+NVP or LPV/r	Refer urgently for alternate triple therapy CD4 <250cells/µl: NVP 200mg daily for 2 weeks, then 200mg BD CD4 ≥250cells/µl LPV/r 2 tablets 12 hourly
Labour		
Unbooked and presents in labour and tests HIV positive Emergency caesarean section in an unbooked woman with no ART	sdNVP + sd Truvada and AZT 3-hourly in labour sdNVP + sd Truvada for C/S Start FDC next day regardless of CD4 cell count	Woman qualifies for lifelong ART Do creatinine and CD4 testing. Woman should get results at the 3-6 days visit
Post-Partum		
Mother diagnosed with HIV within 1 year post-partum or still breastfeeding beyond 1 year	Lifelong FDC initiated immediately	

Figure 4: Algorithm for initiation for ART for HIV-positive women (ART naïve)

For women who are newly diagnosed HIV-positive or are known to be HIV-positive but not yet on ART and are identified at any time during pregnancy, whilst breastfeeding or within 1 year post-partum.

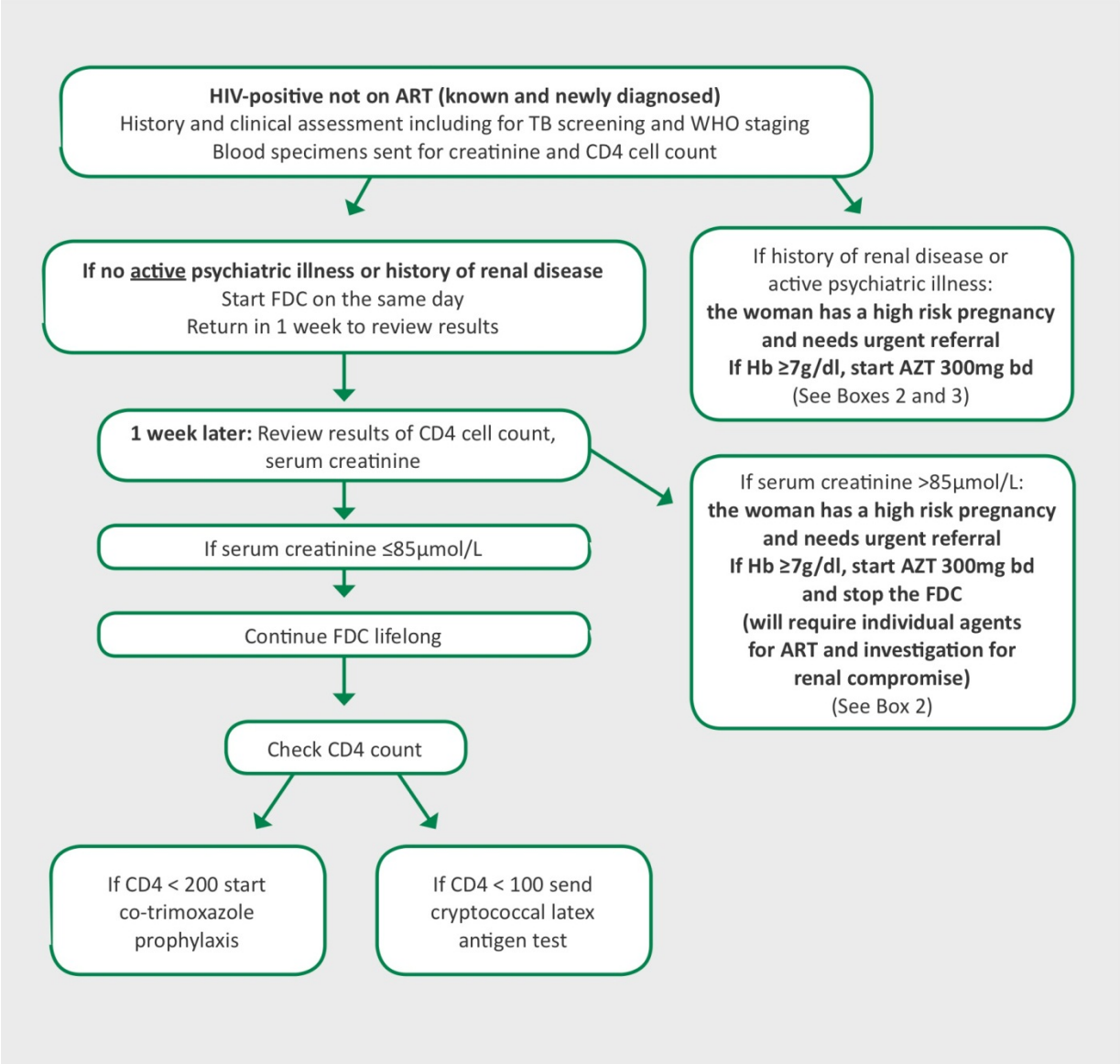
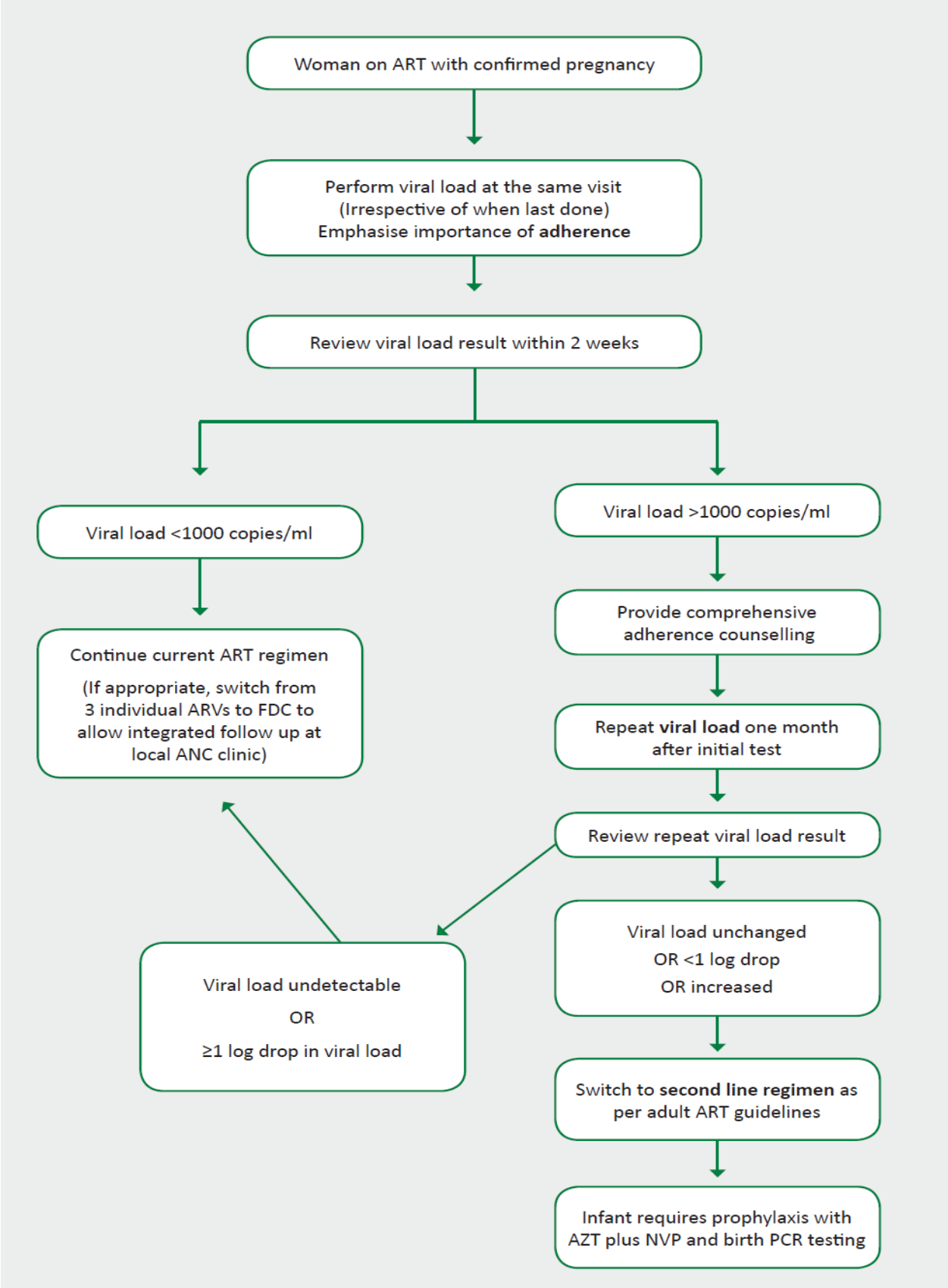


Figure 5: Algorithm for management of pregnant woman already on ART for >3 months



6.1.3 Baseline and routine monitoring for pregnant and breastfeeding women

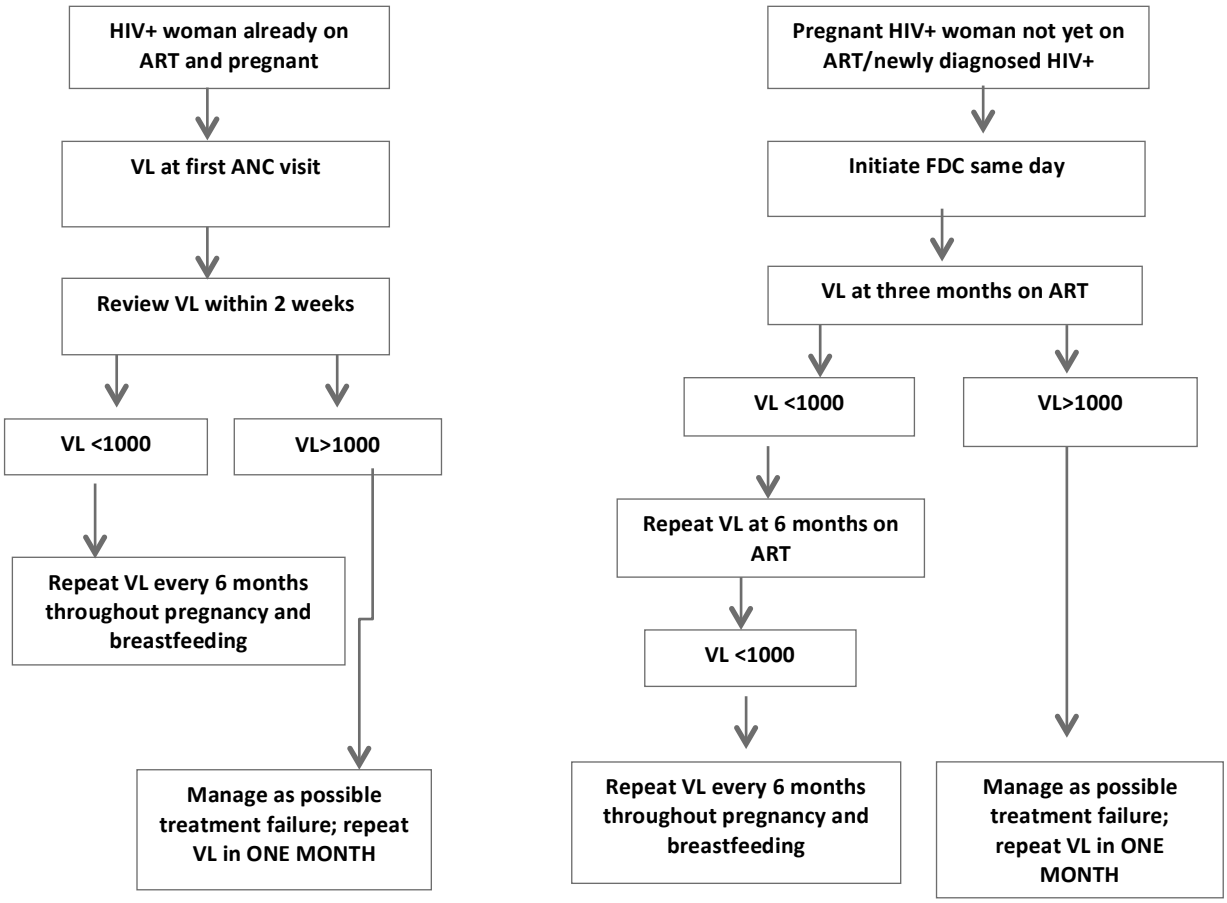
When determining renal function in pregnancy, it is important to note that other methods of estimating renal function, including estimated glomerular filtration rate (GFR) from the Cockroft-Gault equation, are inaccurate in pregnancy. The use of serum creatinine and not the GFR should be used.

Box 12: Standardised baseline monitoring (pregnant and breastfeeding women)

Phase of HIV Management **HIV diagnosis (First ANC visit)**	**Purpose**
Confirm HIV result with rapid antibody test if no test results are available	To confirm HIV-positive status in patients who present without documented proof of positive HIV status
WHO clinical staging if HIV-positive	To assess risk
CD4 count	• To identify eligibility for Cotrimoxazole (CD4<200) • To identify eligibility for CrAg or CLAT (CD4<100) • Not used to determine eligibility if pregnant/breastfeeding or has TB or HIV/Hep B co-infected or has WHO stage IV
VL (Women becoming pregnant while on ART)	• Assessment of effectiveness of treatment and to detect treatment failure • Do VL for all pregnant and breastfeeding women at first visit regardless of when the last VL was done
Screen for chronic diseases (hypertension, diabetes, proteinuria, previous renal disease)	To identify high-risk pregnancy
Nutritional assessment	To detect any nutritional deficiencies and provide appropriate nutrition care and support
Ask about family planning	To provide counselling on safer sex, family planning, postnatal contraception, partner testing and routine cervical cancer screening.
Screen for TB symptoms using the TB screening tool	To identify TB suspects for investigation and to assess eligibility for INH/IPT
Screening for STIs and syphilis	To identify and treat those with STI
Cryptococcal Antigen (CrAg) test if CD4<100	To identify and provide prophylaxis for disseminated cryptococcal infection
Do Hb or FBC Do Creatinine ALT only if requires NVP	To detect anaemia or neutropenia To assess renal sufficiency To exclude liver dysfunction
On ART	**Purpose**
CD4 at initiation and then 1 year on ART, then yearly	To monitor immune response to ART
Do VL at confirmation of pregnancy if already on ART>3 months VL at months 3, 6, 12, 18, 24 throughout pregnancy and breastfeeding	• To identify treatment failures and problems with adherence • To ensure women who conceive on ART are fully suppressed to minimise risk of MTCT • To more actively monitor VL throughout pregnancy and breastfeeding to inform urgent response to detectable VL as this increases risk of MTCT
Alanine transaminase (ALT) if on NVP and develops rash or symptoms of hepatitis	To identify NVP toxicity

Phase of HIV Management	Purpose
FBC at month 3 and 6 if on AZT and then every 12 months	To identify AZT toxicity
Creatinine at month 3 and 6, month 12, then every 12 months if on TDF	To identify TDF toxicity

Figure 6: Algorithm for VL monitoring in HIV-positive pregnant women



6.1.4 Viral load monitoring for first-line regimen in pregnant and breastfeeding women

Table 7: Viral load monitoring for first-line regimens in pregnant and breastfeeding women

Viral Load (VL)	Response
<50 copies/mL	6-monthly VL monitoring and routine adherence support
400-1000 copies/mL	• Assess adherence carefully • If VL≤1000 copies/ml, continue on current ART regimen • Repeat viral load at 6 months, if suppressed, continue with 6 monthly VL testing • If concerns about adherence consider doing another viral load within 6 months • Repeat viral load at 6 months, if suppressed, return to 6 monthly VL testing
>1000 copies/mL	**Pregnant women:** If VL>1000 copies/ml, provide adherence counselling,

Viral Load (VL)	Response
	repeat the VL in 1 month • If second VL result is undetectable or has shown a reduction in viral load of 1 log (10-fold) or greater, continue with the existing regimen • If the VL result is unchanged or has not shown a 1 log (10-fold) reduction or has increased, the woman should be switched to second-line therapy urgently • Any woman who requires a switch to second-line therapy must receive intensive adherence counselling and support to ensure high-level adherence and rapid viral load suppression

Always check for Hepatitis B before stopping TDF. If patient has chronic hepatitis B, stopping TDF may lead to a fatal hepatitis flare. If Hepatitis B outcome is positive, TDF should be continued as a 4th drug in the second regimen.

6.1.5 Recommended second-line regimen for pregnant/breastfeeding women

Table 8: Recommended second-line treatment for patients failing first-line regimen

Second-line regimen	
Failing on a TDF-based 1st line regimen	AZT + 3TC + LPV/r AZT + **TDF** + 3TC + LPV/r (4 drugs if HBV co-infected)
Failing on a d4T or AZT-based 1st line regimen	TDF + 3TC (or FTC) + LPV/r
Dyslipidaemia or diarrhoea associated with LPV/r	Switch LPV/r to ATV/r

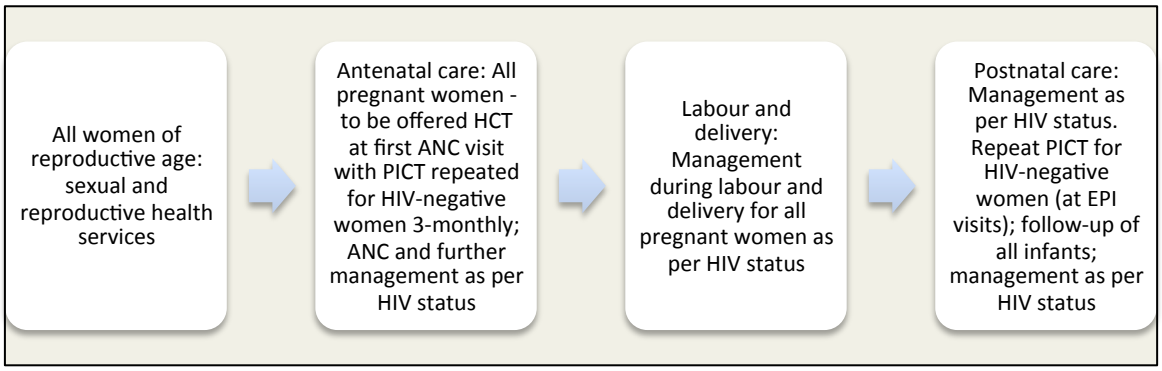
6.2 LABOUR, DELIVERY AND POSTNATAL FOLLOW-UP OF MOTHER AND BABY

6.2.1 Overview of the PMTCT programme

The PMTCT programme aims to reach out to all women before and during pregnancy, through labour and delivery, and through the postnatal period up to 18 months.

The programme aims to identify and promote the health of HIV-positive mothers and their HIV-exposed infants, including the diagnosis, management and prevention of opportunistic infections. The various components of the PMTCT programme are highlighted in Box 13, and the goals and management thereof are summarised according to the woman's HIV status and the infant's HIV exposure.

Box 13: Key components of the PMTCT programme



Mothers are encouraged to exclusively breastfeed their infants during the first 6 months of life, with appropriate complementary foods being introduced from 6 months and breastfeeding continuing for up to 2 years and beyond.

Box 14: PMTCT – Key points to note

- All HIV-exposed infants not on ART should have a rapid test at 18 months of age to confirm HIV status conferred by the 6-week HIV PCR test, or the 16-week HIV PCR performed 4 weeks post the 12-week NVP prophylaxis, or 6 weeks post-cessation of breastfeeding test
- All HIV-positive women should have access to TB symptom screening, INH prophylaxis plus pyridoxine and/or Cotrimoxazole prophylaxis, nutritional and psychosocial support, cervical cancer screening, counselling on and access to family planning options, monitoring of CD4 cell count, viral load and clinical staging
- Mothers of unknown HIV status or who are HIV-negative should be tested 3-monthly, throughout pregnancy, at labour/delivery, at the 6-week EPI visit and 3-monthly throughout breastfeeding. At initial PICT in ANC, mothers will be consenting for the protocol of initial and repeated HIV testing so as to ensure that the tests can be done efficiently without any requirement for further counselling, unless indicated
    - All HIV-positive women who started FDC (TDF+FTC+EFV) or another triple-drug regimen during the antenatal period should continue to receive this regimen throughout labour and delivery
    - Unbooked women in labour or newly diagnosed in labour should be counselled and provided with ART to prevent MTCT, and initiated on lifelong ART before being discharged
    - They should have their CD4 and creatinine checked and reviewed at the 3-6 day postnatal visit
    - Caesarean sections should be done for obstetric indications and are not recommended to reduce MTCT
    - Women who initiated FDC during ANC period should continue this regimen throughout delivery and the postnatal period
    - In an emergency caesarean section, a woman who is not on ART should receive sdNVP and TDF + FTC (Truvada®) as prophylaxis prior to the procedure
    - All HIV-positive women who undergo caesarean section should receive prophylactic antibiotics
    - All women diagnosed HIV-positive within the first year postpartum are to be initiated on lifelong ART regardless of CD4 count or feeding practice

Safer delivery technique: MTCT risk is increased by prolonged rupture of membranes, assisted instrumental delivery, invasive monitoring procedures, episiotomy and invasive suctioning of the neonates nose and airway. These invasive interventions should be avoided in HIV-positive women and their infants. If there is meconium stained liquor this requires laryngoscopy and suctioning under direct vision only for those babies who are flat at birth and require resuscitation. Routine

suctioning of the airways of newborns where there is meconium staining of the liquor is not recommended. Only suction the baby's nose and airway and wipe the neonate carefully at birth if required. Most newborns at birth do not require suctioning.

Caesarean section: All HIV-positive women to receive prophylactic antibiotic and HIV-positive women not on ART must receive sdNVP and TDF + FTS (Truvada©) beforehand.

6.2.2 Immediate post-delivery period

Box 15: Immediate post-delivery period for women

Mother: Immediate post-delivery care	
Mother: Within an hour of delivery	**Before leaving the facility**
• Infants born to HIV-positive women should receive skin-to-skin contact with their mothers almost immediately, regardless of the mother's infant feeding choice • Initiate exclusive breastfeeding immediately or within one hour of delivery • If the mother has decided to exclusively formula feed, she should bring infant formula with her which should be provided within one hour of delivery • Initiate HIV-exposed infants on ARV prophylaxis immediately after birth or very soon after • Discuss contraception options and offer appropriate method to the mother	**All women must be counselled about:** • The need for consistent maternal ART adherence and infant prophylaxis to reduce risk of MTCT • The importance of exclusive breastfeeding for the first 6 months • The dangers of mixed feeding – providing a combination of breast milk plus infant formula, water or other foods or fluids (excluding prescribed medications) within the first 6 months **All women should:** • Be given at least 8 week's supply of ART and 6 week supply for infant prophylaxis on discharge • Follow-up at a health facility within 3-6 days and again 6 weeks post-partum • Have a correctly completed RTH booklet (mandatory) • Have a finalised plan for the mother-baby pair before the pair is discharged after delivery. Mothers and their infants should receive healthcare at the same consultation regardless of service point • Receive documentation regarding mother-baby pair, including referral letters

6.2.3 Care of HIV-exposed infants in the immediate post-delivery period

Box 16: Immediate post-delivery care for infants

- Infants to be vaccinated as per the EPI schedule
- BCG given to all infants, unless mother has active TB or <2months on TB treatment. Exposed infants must be screened for congenital TB. (See Annexure 4)
- ALL HIV-exposed infants must be tested for HIV as per guidance
- ART prophylaxis given at birth to all HIV-exposed infants is effective in reducing MTCT whether maternal ART is received or not. It is also highly effective in reducing MTCT through breast milk
- Infants born to HIV-positive women should receive daily NVP for 6 weeks, unless there are

circumstances that warrant 12 weeks of NVP or NVP plus AZT

- Abandoned babies must receive NVP prophylaxis immediately until HIV-exposure status has been determined, using an HIV antibody test. This applies also in cases in which the mother is indisposed (due to severe illness, coma, mental illness, or death)
- EPI-scheduled visits for vaccination at 6, 10 and 14 weeks at EPI clinic and a routine health check must be performed
- First postnatal visit for the infant is scheduled for day 3, and should occur within 6 days of life at the health facility

Note: Where the mother is known to be HIV-positive, but she refuses any ART prophylaxis for the infant, a counsellor must intervene to explain the risks of MTCT and the benefits of ART prophylaxis and therapy. If this fails to convince the mother to take infant prophylaxis, the mother should then be informed of the infant's right to receive protection from acquiring HIV. The healthcare provider should consult the head of the facility and, with their permission, provide the necessary treatment in the best interest of the infant. In all actions concerning children, the best interests of the child shall be a primary consideration (Children's Act, No. 38 of 2005).

6.2.4 Immediate postnatal care for HIV-positive infant and child

A full plan for the mother-baby pair follow-up should be finalised before the pair is discharged after delivery. Whenever possible, mothers and their infants should receive healthcare at the same consultation regardless of service point. The RTH booklet should be completed prior to discharge after delivery, and should include a record of the HIV treatment received by the mother during pregnancy and postpartum, maternal illnesses, infant HIV prophylaxis and intended feeding method. Women should be provided with clear documentation to take with them to enable them to continue lifelong ART, without interruption, whenever they move to a new healthcare facility. A transfer or referral letter must at the minimum stipulate when ART was initiated, record baseline and monitoring blood results and outline the management plan for both mother and infant.

If a mother/caregiver is concerned about the infant's health, including poor feeding, lethargy or jaundice, they should urgently present to a health care facility.

The first postnatal visit for the infant is scheduled for day 3 but should take place within 6 days of life at a health facility.

Adequacy of breastfeeding must be checked by noting the infant's state of hydration and general condition. Any concerns around infant feeding should be addressed and follow-up sooner than 6 weeks arranged.

6.3 ART PROPHYLAXIS IN HIV-EXPOSED INFANTS

In order to make breastfeeding safer, all HIV-exposed children should receive prophylactic NVP from birth for 6 weeks. If there is no breastfeeding, the infant must take NVP until six weeks of age. In several cases daily NVP will be required beyond 6 weeks (see Table 9 below).

Infant post-exposure prophylaxis should be used for 6-12 weeks after delivery, dependent on when maternal ART was initiated. Some infants will receive dual prophylaxis with NVP plus AZT. After infant prophylaxis has been completed, the mother will continue to breastfeed and reduced MTCT will be reliant on maternal adherence to lifelong ART throughout the breastfeeding period. HIV positive women are recommended to breastfeed until 12 months of age.

6.3.1 When to start: Eligibility criteria for ART prophylaxis in HIV-exposed infants

Table 9: Eligibility criteria for HIV-exposed infants

Mother	Infant regimen	Comment
Mother on lifelong ART	NVP at birth and then daily for 6 weeks	Mother has been on ART for >4 weeks prior to delivery
Mother did not get any ART before or during delivery and tests HIV-positive >72hours post-delivery OR Mother newly diagnosed HIV-positive within 72 hours of delivery OR Mother started ART less than 4 weeks prior to delivery	NVP as soon as possible and daily for 12 weeks (if infant is breastfed)	12 weeks extended NVP is only necessary if the infant is being breastfed. Check feeding practice at the 6 week EPI visit to ensure infant receives correct duration of prophylaxis If mother received no ART before delivery, infant should receive birth PCR An additional HIV PCR test is required 4 weeks after NVP is discontinued This extended period of infant prophylaxis is required to allow time for maternal viral suppression. It takes up to 12 weeks for the viral load to become undetectable on ART
Breastfeeding mother diagnosed with HIV Start mother on a FDC immediately	NVP and AZT immediately If infant tests HIV PCR negative: stop AZT and continue NVP until 4 weeks post-cessation of breastfeeding, unless mother has been on ART for at least 12 weeks. If mother has received 12 weeks of ART then infant NVP can be stopped	Do HIV PCR and return for results in 7 days If infant <6 weeks, repeat HIV PCR at 6 weeks Additional HIV PCR 4 weeks after stopping NVP Infant HIV testing 6 weeks post-cessation of breastfeeding (either HIV PCR or ELISA, depending on age)
Unknown maternal status for any reason, including orphans and abandoned infants	Give NVP immediately* Test infant with rapid HIV test* If positive continue NVP for6 weeks If negative discontinue NVP	If rapid test is positive do a birth PCR and if negative, follow up with a 6-week HIV PCR

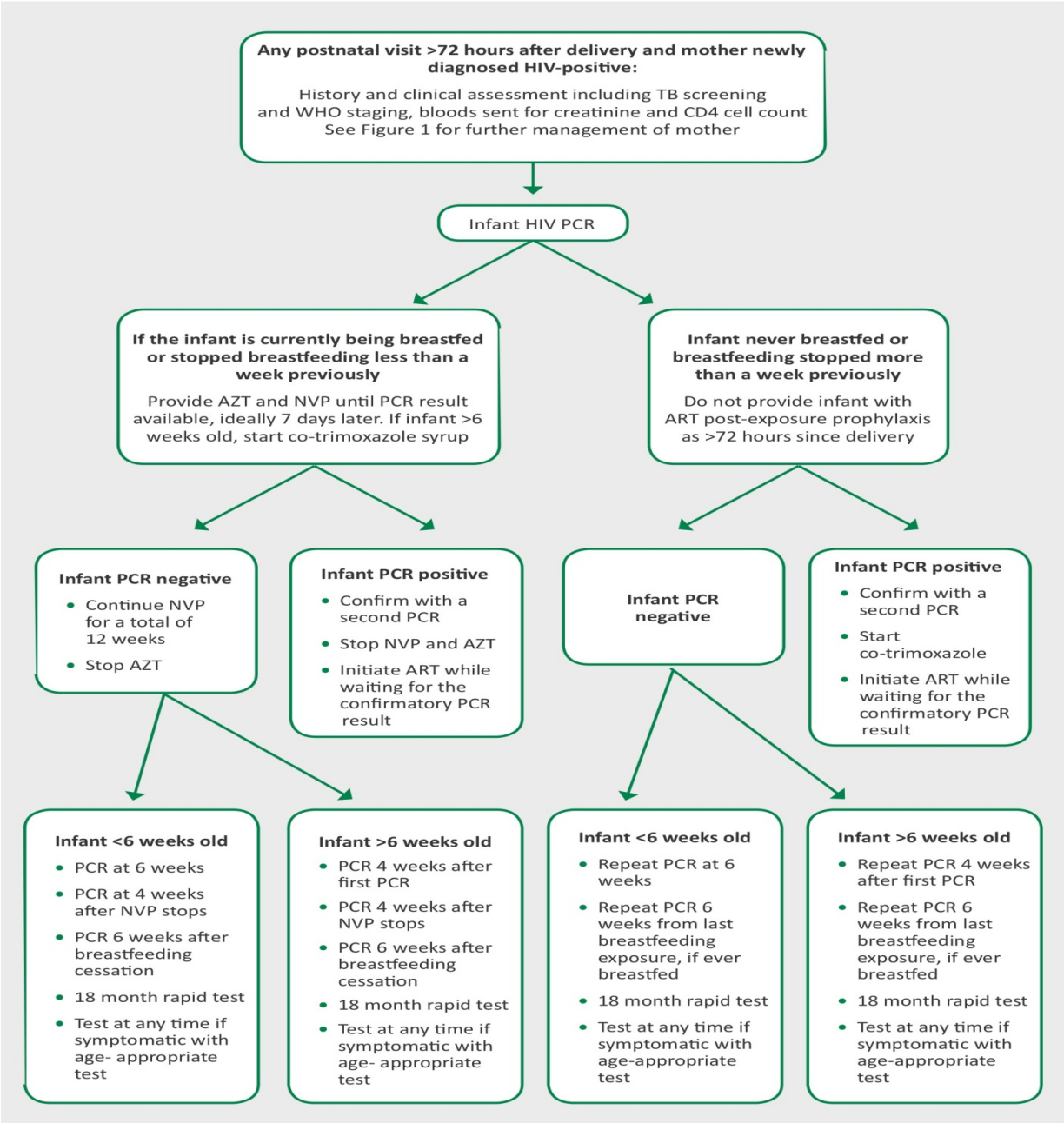
Mother	Infant regimen	Comment
Mother with latest viral load >1000 copies/ml	Dual ARV for 6 weeks (NVP and AZT). Perform an HIV PCR at or shortly after birth	PCR at birth, if negative follow up with a 6 week HIV PCR Manage the mother as per Table 7 If repeat maternal viral load >1000 copies/ml then refer to/discuss telephonically with paediatric expert before the infant is 6 weeks old and prophylaxis is due to be discontinued Infants of mothers on 2nd or 3rd line regimens and VL>1000 should not be breastfed
Non-breastfeeding mother diagnosed with HIV	If more than 72 hours since delivery, no infant NVP Perform an HIV PCR, if positive initiate ART	Do HIV PCR, if <18 months Do rapid test if >18 months, Repeat PCR 6 weeks after last HIV exposure

If rapid HIV test can be done within 2 hours, then wait for HIV result before commencing NVP

Note: Remember to repeat the HIV PCR 6 weeks after breastfeeding cessation for all breastfed infants if < 18 months and a repeat HIV rapid test if > 18 months

Figure 7: Algorithm for initiation of infant prophylaxis or ART >72 hours after delivery

For any woman who is newly diagnosed HIV-positive >72 hours after delivery and is either breastfeeding or within 1 year post-partum



Note: When the child is PCR negative, NVP should be stopped at 12 weeks only if the mother is on ART, and has been for 12 weeks. (Refer to table 9)

6.3.2 When to start: Eligibility criteria for Cotrimoxazole prophylaxis in HIV-exposed infants

All HIV-positive and HIV-exposed infants must receive Cotrimoxazole prophylaxis from 4-6 weeks of age as outlined in Table 10.

Table 10: Pneumocystis Jiroveci Pneumonia (PCP) prophylaxis using Cotrimoxazole

Indications for Cotrimoxazole	When to start	When to stop
All HIV-exposed infants	Start from 4-6 weeks after birth	Stop when PCR negative ≥6 weeks after full weaning *AND* infant is clinically HIV negative
All HIV-exposed exclusive formula feeding children (EFF)	Start from 4-6 weeks after birth	Stop when PCR negative *AND* infant is clinically HIV negative *AND* EFF is expected to continue
All HIV-exposed breastfeeding children	Start from 4-6 weeks after birth	Stop when PCR is negative ≥6 weeks after full weaning *AND* infant is clinically HIV negative
HIV-positive infants <12 months old	Start from 4-6 weeks after birth or as soon as possible after HIV diagnosis even if on ART	All infants <12 months should remain on prophylaxis
For HIV-positive children 1-5 years with or without ART	All symptomatic children (WHO clinical stage 2, 3 or 4) ORCD4 <25% OR<500 cells/µl.	Stop once ART-associated immune reconstitution has occurred for ≥6 months i.e. CD4 percentage ≥25% or CD4 count ≥500 cells/µl on ≥2 occasions, 3-6 months apart
HIV-positive children ≥ 5 years of age with or without ART	Start if CD4 count <350 cells/µl or WHO clinical stage 3 or 4 disease (including TB)	Stop once ART-associated immune reconstitution has occurred for ≥6 months, i.e. CD4 ≥350 cells/µl on ≥2 occasions, 3–6 months apart
Any HIV-positive child with high risk for bacterial infections or at risk of malaria	Start Cotrimoxazole prophylaxis even with ART immune-reconstitution	Do not stop until risk has been eliminated and all CD4 cell percentage or CD4 cell count criteria listed above have been met
HIV-positive child with previous PCP infection	Start as soon as first PCP episode has been treated	Stop at age 5 years if CD4 criteria is met

Note: Any one of the criteria could be used for starting therapy

Recommended doses of Cotrimoxazole by age or weight of child are shown in Table 11.

6.3.3 What to start: Dosing guide for NVP, AZT and Cotrimoxazole in infants

Table 11: Prophylactic Nevirapine (NVP) dosing guide for HIV-exposed infants

NEVIRAPINE DOSING GUIDE			
Drug	**Age or Weight**	**Age/daily dose**	**Volume**
Nevirapine (NVP) Birth – 6 weeks	<2.0kg	Birth to 2 weeks: 2mg/kg 2 to 6 weeks: 4mg/kg	0.2ml/kg
	2.0 – 2.5kg	Birth to 6 weeks: 10mg	1ml
	>2.5kg	Birth – 6 weeks: 15mg	1.5ml
	Any weight	6 weeks to 12 weeks: 20mg	2ml
Nevirapine (NVP) > 6 weeks – 6 months	All	20mg/day	2ml
> 6 month – 9 months	All	30mg/day	3ml
> 9 months	All	40mg/day	4ml

Table 12: Simplified infant AZT dosing birth to 6 weeks

Zidovudine (AZT)	2000 to 2499g	10mg twice daily	1ml twice daily
	>2500g	15mg twice daily	1.5ml twice daily

Table 13: Recommended dosing guide for prophylactic Cotrimoxazole for infants and children

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

Cotrimoxazole can cause erythema multiforme and Stevens-Johnson syndrome. If this occurs, stop the Cotrimoxazole.

Dapsone should be used in Cotrimoxazole intolerant patients. The recommended dose is 2 mg/kg/day or 4 mg/kg/week. The maximum daily dose is 100 mg (1 tablet).

6.4 ART IN INFANTS, CHILDREN AND EARLY ADOLESCENTS

6.4.1 General principles of ART care in infants and children

The goal of ART for children is to increase survival and decrease HIV-related morbidity and mortality.

When a child is on ART:

- The child's CD4 count should rise and remain above the baseline count
- The child's viral load should become undetectable (<50 copies/mL) and remain undetectable

In some children, a suppressed though detectable viral load, with sustained elevation in CD4 count and absence of inter-current and/or opportunistic infection, may be the best achievable goal.

Children should be started on ART as soon they become eligible using the standard drug regimens that have proven efficacy and seldom have serious side-effects. Children who may need non-standard regimens should only have treatment initiated by experienced clinicians. Constant availability of ARVs must be assured and clinicians must be vigilant for drug interactions and monitor patients for the development of resistance and adverse reactions. Adherence is the key to successful therapy, ensure that ongoing support is provided to the patient and family in order to maintain adherence. A minority of patients may not respond to ART and continue to progress in spite of good adherence. This may occur especially in those who are severely ill prior to commencing ART or these who have transmitted viral resistance. Underlying opportunistic infections should be sought and resistance testing may be of value.

Ongoing care for children on ART includes:

- Monitoring treatment response and adherence to ART
- Monitoring growth and developmental milestones
- Providing the necessary ARVs on a regular basis
- Assessment for drug side-effects or other complications
- Provision of routine care e.g. immunisation
- Management of inter-current infections and illnesses
- Counselling and support of the parents/caregivers
- Arranging for palliative care where appropriate, with the support of NGOs
- Consider the child's home as an important factor in his/her care and the conditions must not be overlooked
- Home visits together with a social worker must be encouraged
- Updating the RTH booklet whenever necessary (caregivers to be encouraged to bring it to all visits)

Administration of ARVs

Most ARVs are currently available separately. However, some fixed-dose combinations are already available e.g. 3TC/ABC 300mg/600mg FDC and AZT/3TC 300mg/150mg FDC. In addition other fixed-dose combinations and co-packaged formulations will become available in the near future. These will facilitate dispensing of ARVs, and promote adherence by reducing the number of medicines that patients have to take. The use of FDCs is encouraged and patients are advised to:

- Switch to tablets or capsules from syrups or solutions as soon as possible
- Keep Lopinavir/Ritonavir solution cool (<25ºC), and it should be refrigerated prior to dispensing. It can be kept out of the fridge for 42 days

6.4.2 When to start: Eligibility criteria for ART in infants, children and early adolescents

There must be a confirmation of diagnosis of HIV infection, including the criteria in Table 14.

Table 14: Criteria for initiating ART in children <10 years

<table>
<tr><th colspan="2">CLINICAL CRITERIA</th><th>SOCIAL CRITERIA</th></tr>
<tr><th>Age</th><th>Eligibility for Treatment</th><td rowspan="3">Social criteria are extremely important for the success of the programme and need to be adhered to. The principle is that adherence to treatment must be at least probable.

• At least one identifiable caregiver who is able to supervise the child for administering medication (all efforts should be made to ensure that the</td></tr>
<tr><td>Child less than 5 years</td><td>All children should be started on ART</td></tr>
<tr><td>5 – 10 years</td><td>Symptomatic (stage III or IV) irrespective of CD4 count

OR CD4 <500 cells/µl irrespective of WHO stage</td></tr>
</table>

CLINICAL CRITERIA	SOCIAL CRITERIA
Criteria for fast-tracking (i.e. start ART within 7 days of being eligible) • Children less than 1 year of age • CD4 count <200 cells/µl or <15 % • WHO clinical Stage 4 • MDR or XDR-TB	social circumstances of vulnerable children, e.g. orphans, are addressed so that they too can receive treatment) • Disclosure to another adult living in the same house is encouraged so that there is someone else who can assist with the child's ART • Treatment of mother/caregiver/other family member is to be actively promoted by ensuring same-site treatment or referral to the nearest treatment centre

6.4.3 What to start: First-line ART regimens for infants, children and early adolescents

Standard starting regimens for children initiating ART are shown in Table 15. Doses are based on the child's weight (see ARV Dosing Chart for Children 2013). It is important to regularly check that children receive the correct dose based on their weight. In older children or adolescents ensure that maximum doses are not exceeded.

Table 15: First-line regimens for ART initiation in children

Child	Regimen	Comment
Children <3 years or older children weighing <10kg	ABC + 3TC + LPV/r	Doses are based on child's weight and need to be adjusted as the child grows
Children 3-10 years and>10kg Adolescents 10-15 years or <40kg	ABC + 3TC + EFV Children who started on ABC/3TC/LPV/r before 3 years must remain on same regimen at 3yr	Do not exceed maximum dosage If adolescents weight <40kg, align treatment with children's regimen
Children on d4T	Change all d4T to ABC	If VL suppressed: change to ABC If VL>1000 copies/ml, manage as treatment failure If VL 50-1000 copies/ml, consult specialist
Children on ddI	Change all ddI to ABC	Change all regardless of VL

6.4.4 Baseline and routine clinical and laboratory monitoring for infants, children and early adolescents

Table 16: ART monitoring in infants and children on ART

At initial diagnosis of HIV	Purpose
Verify HIV status	Ensure that national testing algorithm has been followed
Document weight, height, head circumference (<2 yrs) and development	To monitor growth and development + identify eligibility for ART

Screen for TB symptoms	To identify TB/HIV co-infection
WHO clinical staging	To determine if child ≥5years is eligible for ART
CD4 count testing	Children <5 years – Baseline and eligibility for fast-tracking, DO NOT wait for CD4 count to start ART
	Children ≥5 years – To determine eligibility for ART, fast-tracking and start Cotrimoxazole prophylaxis as per national guideline
Hb or FBC	To detect anaemia – do Hb/FBC to detect neutropenia– FBC
At routine follow-up visits (non-eligible patients)	**Purpose**
Document weight, height and development	To monitor growth and development and assess clinical staging
Check that a CD4 count has been done in the last 6 months	To determine if patient has become eligible for ART
WHO clinical staging	To determine if patient has become eligible for ART and CPT
Screen for TB symptoms	To identify TB/HIV co-infection
At initiation of ART (Baseline)	**Purpose**
Hb or FBC	If less than 8 g/dl start ART and discuss with a specialist for opinion
CD4 count (if not performed in last 6 months)	Baseline assessment
Cholesterol + Triglyceride if on PI-based regimen	Baseline assessment
ALT (if jaundice or on TB treatment)	To assess for liver dysfunction
On ART	**Purpose**
Height, weight, head circumference (<2yrs) and development	To monitor growth and developmental milestones
Clinical assessment	To monitor response to ART and exclude adverse effects
CD4 at 1 year into ART, and then every 12 months	To monitor response to ART, stop Cotrimoxazole prophylaxis as per national guideline
VL at month 6, 1 year into ART, then every 12 months	To monitor viral suppression response to ART; To identify treatment failure and to identify problems with adherence
Hb or FBC at month 1, 2, 3 and then annually if on AZT	To identify AZT-related anaemia
Cholesterol + Triglyceride at 1 year and then every 12 months if on PI based regimen	To monitor for PI-related metabolic side-effects
Clinical drug-related adverse events	To identify drug-related adverse events; If develops jaundice or rash on EFV or NVP do Liver function test and refer to specialist

6.4.5 Viral load monitoring and first-line ARV treatment failure for infants and children

Changing a child from first to second-line ARV is a decision that should only be undertaken after careful consideration and discussion (even telephonically) with an expert. Second-line treatment is generally used following **treatment failure, as reflected by a VL greater than 1000 copies/mL despite good adherence**. General considerations prior to defining treatment failure:

- Allow reasonable trial on therapy with good adherence (at least 12 – 24 weeks) before concluding that a regimen is failing. Monitor adherence closely during this time

- Once treatment failure is identified, changes should be made within 6 months. There is little purpose in leaving a child on a failing regimen for an extended period of time
- Always attempt to improve adherence before switching regimens, as poor adherence to treatment is the most common cause of virological failure
- If it is not possible to improve adherence:
    - Treat any inter-current opportunistic infections
    - Holding strategies or Directly Observed Therapy (DOT) may be attempted. DOT can be done with a healthcare worker or the trusted 'other' family member or friend
    - Exclude Immune Reconstitution Inflammatory Syndrome (IRIS)
    - Ensure adequate nutrition

Table 17: Viral load monitoring and recommended responses

Viral load (VL)	**Response**
< 50 * copies/mL	12-monthly VL monitoring and routine adherence support
50*-1000 copies/mL	Repeat VL in 6 months Begin step-up adherence package if VL still between 50* – 1000
> 1000 copies/mL	Begin step-up adherence package Repeat VL in 3 months If <50*, return to routine VL monitoring as above If between 50 and 1 000, continue step-up adherence and repeat VL after 6 months If >1 000, despite stepped up adherence support, AND child is on an NNRTI-based regimen, discuss with expert regarding new regimen. <u>If >1000 and child is on a PI-based regimen:</u> Reinforce adherence (very difficult to fail a PI-based regimen unless the child received unboosted PI or was on rifampicin containing TB treatment while on a PI) Discuss with an expert regarding new regimen if VL >30 000, If the child received an unboosted PI (e.g. ritonavir alone) in the past or received TB treatment while on an LPV/r regimen and the VL is >1000 copies/mL, discuss with an expert regarding new regimen. Resistance testing is indicated in these situations but should only be done if the child has been reliably taking their ARVs in the past month.

***Use 400 copies/ml if laboratory does not test down to 50 copies/ml**

6.4.6 Second-line regimens in infants, children and early adolescents

Children may occasionally need to change a drug from the first-line regimen to one from the second-line regimen, because of intolerance or a serious adverse reaction. Switching limits the patient's second-line treatment options. The decision to switch must be made by a doctor with ARV experience. Switching of one drug should only be done if there is full viral suppression, failing which the whole regimen may need to be altered.

Table 18: Second-line ART regimens for children

Second-line regimen	
Failed first-line protease inhibitor (PI) based regimen	
Failed first-line PI-based regimen	**Recommended second-line regimen**
ABC + 3TC + LPV/r	**Consult with expert for advice**
d4T + 3TC + LPV/r	
Unboosted PI based regimen	
Failed first-line NNRTI-based regimen (discuss with expert before changing)	**Recommended second-line regimen**
ABC + 3TC + EFV (or NVP)	AZT + 3TC + LPV/r
d4T + 3TC + EFV (or NVP)	AZT + ABC + LPV/r

6.4.7 Third-line ART regimens

Children who fail second-line treatment should be referred to an expert so that the treatment with third-line agents can be considered.

6.4.8 General care of HIV-exposed infants and HIV-positive infants and children

Box 17: Identifying children with HIV infection

It is important to identify children who are HIV-positive at an early stage to ensure that they and their families obtain optimal care. The disease progresses more rapidly in children than in adults and therefore children may be the first in the family to fall ill.

Early identification/diagnosis makes it possible to:

- Plan regular follow-up and initiate ART when indicated
- Ensure children receive routine preventive health interventions (immunisation, growth monitoring and promotion, Vitamin A supplementation)
- Prevent opportunistic infections – especially through the provision of Cotrimoxazole prophylaxis
- Identify and treat inter-current illnesses early and effectively, such as TB
- Establish whether any other members of the family are HIV-positive and provide appropriate treatment
- Provide psychosocial support to the family/caregiver through counselling and support
- Facilitate access to social grants, income generation opportunities and other support structures

Constant vigilance is essential in order to ensure that all children who are HIV-positive are identified as early as possible. The possibility of HIV infection should be considered during every contact with the health system, whether at PHC, district hospital or referral level.

Box 18: Proactive steps to detect children with HIV infection

- PMTCT records should identify all HIV-exposed and HIV-positive children
- Children in whom maternal HIV status is unknown must be tested for HIV
- The IMCI case management process includes consideration of possible HIV infection in all children who present to PHC facilities. Correct application of the IMCI case management process would therefore result in identification of almost all HIV-positive children
- Children with pneumonia (especially severe pneumonia), malnutrition and TB must be tested for HIV
- Siblings of children diagnosed as HIV-positive should be tested
- Orphans and abandoned children are at special risk of HIV infection and their HIV status should be established
- All adults testing positive during HCT need to be asked to bring their children for testing
- All adults being tested for HIV when diagnosed with TB need to also bring their children in for both HIV and TB screening

Care for a child with possible or confirmed HIV infection

Caring for a child who is suspected to have HIV infection includes PMTCT follow-up, confirmation of the HIV status and referral for ART if eligible, provision of regular follow-up and preventive care, provision of Cotrimoxazole prophylaxis and the additional preventive care offered to the child.

The child's HIV status needs to be confirmed with a second, age appropriate, confirmatory test.

If a child tests positive for HIV, the following steps should be followed:

- The child should be clinically staged and baseline bloods (CD4 count and percentage, Hb and lipogram) done
- The child's eligibility for ART should be assessed using the criteria in Table 14
- If eligible, ART should be started as soon as possible, especially in infants
- If child is not eligible for ART, regular follow-ups which include regular reassessment of ART eligibility using staging and laboratory criteria must be done at least six monthly, and more frequently if the child is sick or is not thriving

Whilst initiation of ART is important, other aspects of care, such as ensuring that the child receives routine preventive care such as immunisation and growth monitoring and promotion, should not be neglected. These should be provided through regular follow-up visits, as outlined below.

Growth monitoring, promotion and immunisation

Growth faltering is an important indicator of disease progression in HIV-positive children. In children receiving ART it may be an early sign of treatment failure.

- Weight must be recorded on the child's RTH booklet or for children older than 5 years on their weight-for-age chart in the child's clinic file
- Growth faltering must be assessed by means of careful examination for evidence of infections such as respiratory, gastrointestinal or urinary tract infections or TB
- Feeding advice and food supplementation (see Nutritional Support) should be provided
- HIV-positive and HIV-exposed children should be immunised according to the EPI schedule (Table 3 in Section 3.6.3)
- BCG should routinely be given at birth. However, if BCG is delayed because the mother has TB, the HIV-uninfected, exposed infant may receive BCG after completion of prophylaxis. The HIV-positive infant should not receive BCG until he is on ART and has some immune recovery. **BCG should not be given after 1 year of age**

Routine treatments

It is important to ensure that HIV-positive children receive regular routine treatments such as Vitamin A supplementation, Cotrimoxazole prophylaxis from six weeks of age and deworming medication. The recommended schedules are shown in Tables 19 and 20.

Table 19: Vitamin A supplementation

Target group	Dosage	Schedule
All infants 6to11months	100,000IU	Asingledoseattheageofbetween6 and11months(preferablyat9monthswhenchildcomesforimmunisation)
All children 1 to 5 years	200,000IU	Asingledoseat12monthsandthenevery6monthsuntiltheageof5 years

Table 20: Routine deworming

Age	Weight	Mebendazole
12 up to 24 months	<10kg	100mg twice a day for 3 days every six months
>24 months	10kg or more	500mg as a single dose every six months

Additional preventive care for HIV-positive children

Normal transplacental transfer of antibodies from the HIV-positive mother to the child may be impaired and neutrophil function depressed. The infant is therefore at greater risk of developing measles, TB and infections due to encapsulated organisms (*Haemophilus influenzae* and pneumococcus) at a young age.

This can be addressed by:

- Giving additional immunoglobulins to children who have been exposed to measles (measles immunoglobulin is not presently available)
- Varicella immunoglobulin (VZIG) is recommended for children who have been exposed to chickenpox. VZIG should be given as soon as possible after exposure to chicken pox or shingles, but within 96 hours for maximum efficacy. The varicella vaccine can be used both as prevention and as post-exposure prophylaxis if given within 3 days post-exposure
- The influenza vaccine should be given yearly in all HIV-positive children >6 months of age
- Every child should be immunised according to the EPI schedule (Table 3, Section 3.6.3)

6.4.9 Management of children who are not eligible for ART

- Assess the child at least 6 monthly and preferably every 3 months
- CD4 count 6-monthly and WHO staging at every visit
- Document weight, height and developmental milestones
- Prescribe Cotrimoxazole prophylaxis if eligible
- Screen for TB symptoms and investigate if necessary
- Assess for IPT eligibility
- Treat inter-current infections
- Ongoing counselling and continue process of disclosure
- Ensure health of entire family

- Reassess for ART eligibility at each visit. Children who become eligible must be identified early and initiated

6.5 ART FOR ADOLESCENTS 10-15 YEARS

Adolescents fall within the age range 10-19 years according to the WHO. These guidelines apply to any adolescent living with HIV (ALHIV). Adolescents may fall into either the perinatally infected or behaviourally infected category, however in terms of combination ART there would be no difference in approach between these groups.

6.5.1 When to start ART in adolescents 10-15 years and <40kg

ART eligibility criteria

Criteria for initiation

- WHO stage 3 or 4
- CD4 count ≤500 cells/µl

Fast-tracking (initiating ART within 7 days of being eligible)

- CD4 count of ≤200 cells/µl
- WHO stage 4 disease
- MDR/XDR-TB

6.5.2 What to start: ART first-line regimen for adolescents 10-15 years

First-line regimen		
Adolescent	**Regimen**	**Comment**
Weight <40 kg or age <15 years	ABC + 3TC + EFV	NVP can be used if EFV is contraindicated Use TDF if Cr clearance is >80mL/min with no proteinuria If <80 mL/min, use ABC/3TC/EFV and adjust dosages according to renal dysfunction, and discuss with expert
Weight ≥40 kg and age ≥15 years	TDF + 3TC/FTC + EFV (Use FDC)	

6.5.3 Second-line regimen for adolescents 10-15 years

Table 21: Second-line ART regimens for adolescents 10-15 years

Second-line regimen: Adolescents <15 years and <40kg		
First-line virological failure	**Drugs**	**Comment**
ABC/TDF + 3TC/FTC + EFV	AZT +3TC + LPV/r	• Virological failure is 2 consecutive VL>1000 copies/mL that are more than 1 month apart • If VL >1000 copies/mL: o Include intensified adherence for a month o Then repeat VL after 3 months of elevated VL o If VL remains >1000 copies/ml on NNRTI
d4T + 3TC + EFV	AZT + ABC + LPV/r	

		regimen or 10,000 copies/ml on PI regimen, then treat as virological failure • Never switch only one drug in a failing regimen and do not continue therapy with a failing NNRTI regimen for prolonged periods as there is an increased risk of accumulating NRTI resistance mutations

6.5.4 Second-line treatment failure and third-line regimen in adolescents 10-15 years

Table 22: Second-line treatment failure and third-line regimen for adolescents

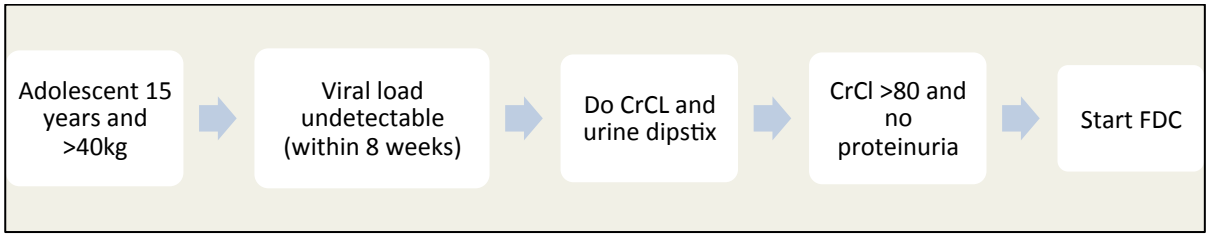
Third-line regimen	
Failing any second-line regimen	Refer for specialist opinion – Regimen based on genotype resistance testing, expert opinion and supervised care Access to third-line ART will be managed centrally by the National Department of Health

6.6 ART IN LATE ADOLESCENTS AND ADULTS

6.6.1 Transition from paediatric ART regimens to adolescent/adult regimens

- Adolescents with an undetectable VL (<50 copies/mL) and no side-effects on ABC + 3TC + EFV can remain on the same regimen until the patient becomes eligible for the TDF + FTC + EFV (FDC) at 15 years old and weighing ≥40kg
- When an adolescent with an undetectable viral load (within the last 8 weeks) reaches 15 years of age and is >40kg, a Creatinine Clearance (Cr Cl) and urine dipstix should be performed
- If the Cr Cl is >80mL/min and no proteinuria on urine dipstix, then the patient can be switched to the FDC (TDF + FTC + EFV)
- If the Cr Cl is <80mL/min or >1+ proteinuria on urine dipstix then refer to an expert for advice before switching

Diagram 2: Transition from child-adolescent regimen



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.

6.6.2 General management of adolescents and adults on ART

Creatinine Clearance

TDF can only be used in patients with creatinine clearance >50 mL/min and creatinine <100 µmol/L.

While the serum creatinine gives an indication of renal function, patients can have significantly reduced renal function with a serum creatinine in the high normal range. This is particularly the case in **older people** and those with **low body weight** where the serum creatinine is a poor indication of renal function.

It is essential to calculate the creatinine clearance in all patients with:

- Age >50 years
- Weight <50kg
- Serum creatinine >100 µl/L
- Co-morbidities that may affect renal function, such as hypertension or diabetes
- Patients that are taking drugs that impair renal function

In all other patients where serum creatinine is <100 µmol/L, the calculated creatinine clearance is likely to be >50 mL/min, and they can safely start Tenofovir.

Creatinine may be elevated in acute illness, and repeating the measurement when the patient is recovered may give a better reflection of clearance.

In patients with **renal impairment**, it may be necessary to reduce the dosage of some ARVs. As renal function improves, do not forget to readjust the dosages accordingly, to ensure patients are not on suboptimal ARV dosage, putting them at risk of virological failure.

Initiating patients on NVP

Patients on NVP must be seen in the first two weeks after initiation of ART, in addition to their regular schedule for monitoring. NVP dosing must be 200mg daily for first two weeks, thereafter 200mg twice daily (BD).

- NVP reactions may be more common at higher baseline CD4 counts, especially in women with CD4 >250 cells/µl, or men with CD4 counts >400 cells/µl. Avoid giving NVP to these patients
- NVP related adverse events occur in the first 3 months of therapy, especially in the first few weeks, and can be fatal; all patients should be warned to return to clinic immediately if they develop a rash, any significant mucocutaneous reactions, fever, jaundice or abdominal pain. Patients with any severe symptoms, or more than two of the above, require immediate hospitalisation with investigation and monitoring. ART, particularly NVP should be interrupted in these cases
- Monitor ALT levels according to symptoms; check ALT in all cases of rash, as concomitant hepatotoxicity may occur. Note that ALT often becomes elevated after the rash has started, so it is important to repeat the ALT after 7-14 days in patients without a significantly elevated ALT at the time the rash develops
- Ensure correct dosing change at 2 weeks. Do not increase the dose to 200 mg BD in the presence of a rash. Delay increase until the rash stabilises. If it does not resolve within a week or worsens, stop NVP and switch to an alternative drug
- While side effects in the first three months can be severe, long-term NVP is very safe. Any patient started on NVP with no side-effects should not be changed to another drug unless virological failure occurs, or if the patient requests to change or for simplification

- NVP should only be used in patients in whom the benefit of use far outweighs the risks associated with using NVP

6.6.3 Immune Reconstitution Inflammatory Syndrome (IRIS)

- IRIS occurs when improving immune function unmasks a previously occult opportunistic infection which subsequently presents with an unusually aggressive inflammatory presentation, or causes paradoxical deterioration of an existing opportunistic disease
- Patients with advanced HIV disease, particularly those with a CD4 count <100 cells/µl, may become ill with IRIS, usually during the first 3 months of ART
- Most cases can be managed on an outpatient basis with disease-specific therapies and anti-inflammatories. Very ill or complex patients may need to be referred for advice regarding investigation and management
- TB is the most common IRIS reaction in South Africa. Some patients starting ART when on treatment for TB will experience recurrence of their TB symptoms/signs or worsening or new manifestations
- The most common of these presentations is with enlarging lymph nodes, often with extensive caseous necrosis. In addition, lung infiltrates or effusions may worsen. It is important to exclude multi-drug resistance(MDR) TB in all these cases, as well as non-adherence to TB medication
- MDRor Extensively drug resistant tuberculosis (XDR) TB needs to be excluded before paradoxical IRIS is diagnosed. TB culture of sputum, blood, lymph nodes and other affected tissue is essential
- Opportunistic infections may also present in atypical ways during this phase of immune reconstitution
- Rashes (including zoster, herpes, molluscum and others), cryptococcal meningitis, and hepatitis due to hepatitis B/C that occur in the first weeks and months of ART initiation are other manifestations of IRIS

Note: IRIS is not indicative of drug failure or drug side-effects. It is not a reason to stop ART, or to change the ARV regimen. However, careful counselling is needed to ensure that the patient understands this.

6.6.4 When to start: ART eligibility in late adolescents ≥15 years and adults living with HIV

Box 19: ART eligibility criteria

Eligible to start ART
CD4 count ≤500 cells/µl irrespective of clinical stage (Prioritise those with CD4 <350 cells/µl) OR Severe or advanced HIV disease (WHO clinical stage 3 or 4), regardless of CD4 count OR Irrespective of CD4 count or clinical stage: • Active TB disease (including drug-resistant and EPTB) • Pregnant and breastfeeding women who are HIV-positive • Known hepatitis B viral (HBV)co-infection • Prioritise those with CD4 ≤350 cells/µl or advanced HIV disease

Timing of ART initiation
• ART should be started as soon as the patient is ready, and within at least 2 weeks of CD4 count being done • In TB co-infection, start with TB treatment first, followed by ART as soon as possible and within 8 weeks • If CD4 <50 cells/µl initiate ART within 2 weeks of starting TB treatment, when the patient's symptoms are improving and TB treatment is tolerated • If CD4 >50 cells/µl initiate ART within 2-8 weeks of starting TB treatment • In cryptococcal or TB meningitis: Defer ART initiation for 4-6 weeks IMMEDIATE INITIATION: All HIV-positive pregnant or breastfeeding women, as long as no active TB FAST TRACKING (within 7 days:) • Patients with CD4 <200 cells/µl • HIV stage 4, even if CD4 is not yet available

6.6.5 What to start: ART first-line regimen for adolescents ≥15 years and adults

Table 23: ART regimens for adolescent and adult pregnant and breastfeeding women

POPULATION	DRUG	COMMENTS
Adolescents >15 years and weighing >40kg Adults All TB co-infection All HBV co-infection	TDF + 3TC (or FTC) + EFV provide as fixed-dose combination (FDC)	Replace EFV with NVP in patients: • With significant psychiatric co-morbidity or intolerance to EFV • Where the neuropsychiatric toxicity of EFV may impair daily functioning, e.g. night shift workers
Adults and adolescents on d4T	Change d4T to TDF (No patient must be on d4T)	Switch to TDF if virally suppressed and the patient has normal creatinine clearance, even if d4T well tolerated If VL>1000 copies/mL, manage as treatment failure and consider switching to second line
Adolescents <15 years or weight <40kg	ABC + 3TC + EFV	If adolescent weight <40kg, align with paediatric regimen
CONTRAINDICATION	**SUBSTITUTION DRUG**	**COMMENTS**
Contraindication to EFV: • Significant psychiatric co-morbidity • Intolerance to EFV • Impairment of daily function (shift workers)	TDF + FTC (or 3TC) + NVP or LPV/r	IfCD4 <250 females and <400 males, give NVP 200mg daily for 2 weeks, then 200mg BD CD4 ≥250 females and ≥400 males, use LPV/r 2 tablets 12 hourly
TDF contraindication: Creatinine clearance of <50 mL/min	ABC+ 3TC + EFV (or NVP)	Renal disease or the use of other nephrotoxic drugs e.g. aminoglycosides MDR treatment

The modified Cockroft-Gault equation:

$$\textbf{Creatinine clearance} = \frac{(140 - \text{age}) \times \text{ideal weight}}{\text{serum creatinine}}$$

*For women, multiply the total by 0.85

Baseline and routine clinical and laboratory assessment for late adolescents and adults

Table 24: Standardised baseline monitoring (all adults/adolescents/pregnant and breastfeeding women)

Phase of HIV management	Purpose
HIV diagnosis	
Confirm HIV result with rapid antibody test if no test results are available	To confirm HIV-positive status in patients who present without documented proof of positive HIV status
WHO clinical staging if HIV-positive	To assess eligibility for ART and timing of initiation
CD4 count	To identify eligibility for ART (CD4 <500/µl) To identify eligibility for prioritisation (CD4 <350/µl) To identify eligibility for fast-tracking (CD4 <200/µl) To identify eligibility for Cotrimoxazole (CD4 <200/µl) To identify eligibility for CrAg or CLAT (CD4 <100/µl)
Screen for pregnancy or ask if planning to conceive	To identify women who need ART for PMTCT and offer appropriate family planning
Assessment of hypertension and diabetes with blood pressure and urine glycosuria	To identify any concomitant chronic diseases
Screen for TB symptoms using the TB screening tool	To identify those suspected of TB and refer them for investigation and to assess eligibility for INH
Screen for HBV (HBsAg)	To identify those co-infected with HBV so that they can be initiated on ART regardless of CD4 count
Screening for STIs and syphilis	To identify and treat STIs
Weight and height in adolescent	To check if the weight is above or below 40kg to determine which ARV drugs to use
Cryptococcus Antigen (CrAg) test if CD4 <100 cells/µl	To assess if there is disseminated Cryptococcal infection and if fluconazole treatment/prophylaxis is indicated
Do Hb or FBC if requires AZT Creatinine if requires TDF ALT if requires NVP	To detect anaemia or neutropenia To assess renal sufficiency To exclude liver dysfunction
Fasting cholesterol and triglycerides if requires LPV/r	To identify at risk of LPV/r related hyperlipidaemia. If above 6 mml/L, consider (ATV/r) instead of LPV/r (if available)
On ART	**Purpose**
Screen for TB symptoms at each visit	To identify TB/HIV co-infected
WHO clinical staging at every visit	To identify new OIs
Ask about side effects at each visit	To identify ARV related toxicity
CD4 at 1 year on ART	To monitor immune response to ART
VL at month 6, month 12 on ART and then every 12 months	To identify treatment failures and problems with adherence
ALT if on NVP and develops rash or symptoms of hepatitis	To identify NVP toxicity
FBC at month 3 and 6 if on AZT and	To identify AZT toxicity

Phase of HIV management	Purpose
then every 12 months	
Creatinine at month 3 and 6, month 12, then every 12 months if on TDF	To identify TDF toxicity
Fasting cholesterol and triglycerides at month 3 if on LPV/r	To identify LPV/r toxicity

6.6.6 Viral load monitoring and first-line ARV treatment failure in late adolescents>15 and adults

Consider switching patients on the first-line drug regimen if the patient has experienced virological failure (VL>1000 copies/mL) on at least two occasions two months apart despite good adherence.

All patients being assessed for switching should have their hepatitis B status checked, especially if on TDF and 3TC/FTC. Withdrawal of TDF can be associated with severe hepatitis in chronic hepatitis B patients (hepatitis B surface antigen positive).

- Check cholesterol, if above 6mmol/l, give Atazanavir/r instead of LPV/r (if available).

Table 25: Viral load monitoring for first-line regimens

Viral Load (VL)	Response
NOTE: Always check hepatitis B before stopping TDF. If patient has chronic hepatitis B, stopping TDF may lead to a fatal hepatitis flare. If hepatitis B positive, TDF should be continued as a 4th drug in the second-line regimen	
<400 copies/mL	• VL monitoring according to duration of ART and routine adherence support • Continue routine VL monitoring as it may be 12 monthly depending on how long patient is on treatment
400-1000 copies/mL	• Assess and manage adherence carefully • Repeat VL in 6 months and manage accordingly
>1 000 copies/mL	• Adherence assessment and intense adherence support • Repeat VL in 2 months and check HBV status and Hb, if not already done • If <1000 copies/mL, repeat in 6 months and then reassess • If >1000 copies/mL and adherence issues addressed, switch to second line therapy after checking HBV status and Hb

6.6.7 Second-line regimen for late adolescents and adults

Table 26: ART regimens

Second-line regimen: adolescents ≥15 years and adults		
First-line virological failure	**Drugs**	**Comments**
Failing on a TDF-based first-line regimen	AZT + 3TC + LPV/r AZT + **TDF** + 3TC + LPV/r (If HBV co-infected)	If non-adherent, address causes of non-adherence If the VL >1000 copies/mL at any point, intensify adherence and
Failing on a d4T or AZT-based first line regimen	TDF + 3TC (or FTC) + LPV/r	

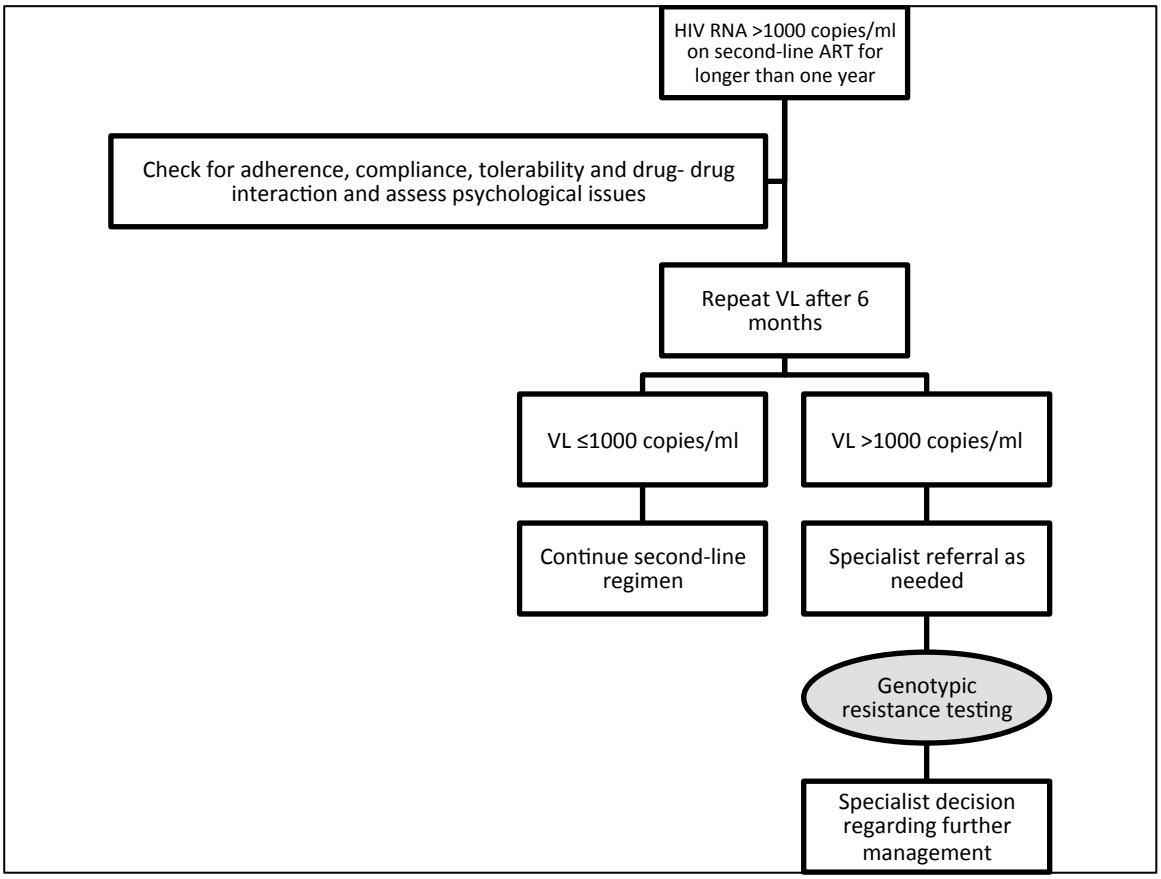
Second-line regimen: adolescents ≥15 years and adults		
Dyslipidaemia (total cholesterol >6 mmol/L) or diarrhoea associated with LPV/r	Switch LPV/r to ATV/r	repeat VL in 2 months If VL remains at >1000 copies/mL after 2 months, then switch to second line regimen
Anaemia and renal failure	Switch to ABC	

6.6.8 Second-line treatment failure and third-line regimen in late adolescents and adults

South Africa has a public health approach to HIV treatment with standardised first and second-line regimens based on efficacy, safety and tolerability. In addition, there are predictable resistance mutations that develop after first-line failure, therefore the second-line therapy selected should achieve viral suppression.

There is a **third-line review committee** that has been set up to coordinate the management of patients failing on the second-line regimen. It has determined that all adult patients who have been on a protease inhibitor (PI) containing regimen for at least a year and have not achieved viral suppression, would be eligible for a genotype to determine if third-line was necessary. Should resistance to a boosted PI be identified, a full treatment history must then be submitted to the committee via the National Department of Health for consideration. Once consensus is reached, a decision is conveyed to the local facility and if third-line is indicated, the drugs are sent to the facility on a named patient basis.

Figure 8: Algorithm for diagnosis of second-line treatment failure



Access to third-line ART is limited to patients who have documented resistance to the PIs they are currently taking. If PI resistance mutations are present then Darunavir-Ritonavir is authorised by an

expert committee, together with Raltegravir and Etravirine and possibly other ARVs depending on the resistance profile and patient ART history.

Box 20: Third-line regimen for late adolescents and adults

Failing any second-line regimen Decision should be based on expert consultation and genotype resistance, and supervised care	Most likely regimens may contain: Raltegravir, Darunavir/Retravirine adjusted according to genotype interpretation and patient history	An expert panel will manage patients failing on second-line therapy. The drugs for third-line will be managed centrally. Should take into account prior exposure and predictable mutations

6.6.9 Management of patients previously on ART

If a patient is referred in (e.g. from the private sector), and **is still on ART**and the regimen is successful (VL undetectable and no side-effects), where possible, the patient should be continued on the same regimen.

If the patient **has interrupted treatment** and was on a previous regimen as above, or where the prior regimen is unknown, take a full history to establish why the treatment was stopped. If the interruption was NOT due to toxicity or clear virological failure, check the VL and restart first line treatment as above, and **repeat the VL after 2 months.**

If patients **have failed a previous regimen**, initiate appropriate second line treatment.

If patient was **previously on ART but has interrupted treatment,** establish the cause of the interruption. If it is due to social or psychological factors, address these and follow up on interventions. If the patient stopped as a result of side effects, evaluate other drug choices and offer appropriate options. If the interruption was due to drug supply issues, and there were no non-adherence, resistance or toxicity issues, the previous ART regimen should be reinitiated as soon as possible.

NB: If NVP is restarted after an interruption of >1 week, re-commence with the 2 week lead-in dose and check the ALT if the patient becomes symptomatic.

7 ARV DRUG INTERACTION, TOXICITY, SUBSTITUTION AND SWITCHING

- ARVs commonly have side-effects and occasionally serious adverse events (SAEs) can occur. However, side-effects are far less common in children than in adults
- Side-effects or adverse events are those reactions to drugs that are known to occur and would be listed in the package insert e.g. nausea, abdominal pain, vomiting etc. Life threatening episodes would be referred to as serious adverse events
- Mild side-effects include mild nausea, vomiting, diarrhoea, dizziness, general malaise, peripheral neuropathy and nail discolouration
- Generally it is recommended that patients continue with the medication if the side-effects are mild
- Adverse events should be recorded and reported regularly to the National HIV and AIDS Cluster. Serious adverse events (SAEs) should be reported within 48 to72 hours (Grade 4 or death) to the Medicines Control Council. After the patient has recovered from the adverse event, it may be possible to recommence therapy with a different regimen. The decision to recommence therapy should be done in consultation with a treatment expert
- **Grading of adverse events:** All adverse events are graded from grade 1 to grade 4 depending onthe severity of theevent as well as the age of the child
- **Response to adverse events:**
    - Grades 1 and 2: Continue with treatment and repeat the test. Reasses the patient within 2 weeks
    - Grade 3: Requires that the test be repeated within 1 week and if it still remains at grade 3, all ARVs must be stopped and patient managed with the assistance of a specialist
    - Grade 4: Requires that all drugs be stopped immediately and be referred to hospital. Thepatient can restart therapy after getting better, and if the same grade 4 occurs again, then the drug must be withdrawn and substituted
- Management of adverse events requires an individualised approach
- If there is a need to discontinue ART, it is advisable to discontinue all ARVs rather than continuing with one or two agents alone. When a patient discontinues a NNRTI-containing regimen, attempt to continue the NRTI component for 2 days after stopping the NNRTI

Remember: Complete an adverse event form and to submit the form to the local pharmacy service

7.1 ARV DOSING AND SUBSTITUTION IN INFANTS AND CHILDREN

See Annexure 5.

7.2 ARV DOSING AND SUBSTITUTION IN ADOLESCENTS AND ADULTS

Table 27: ARV treatment dosing guide for adolescents and adults

ARV adult dosing guide and substitution drugs			
Drug	**Dosage**	**Comments**	**Replacement drug**
TDF (Tenofovir)	300mg daily	TDF is contraindicated if serum creatinine >85µmol/L during pregnancy, or creatinine clearance of <50mL/min in non-pregnant adults	ABC
d4T (Stavudine)	Discontinue use		TDF
3TC	300mg daily		

ARV adult dosing guide and substitution drugs			
(Lamivudine)			
FTC (Emtricitabine)	200mg daily		
NVP (Nevirapine)	200mg daily X 14 days, then 200mg twice daily **In unbooked women in labour, sdNVP is used as a 200mg tablet**	Use with caution in TB treatment Avoid NVP if CD4 count >250cells/µl for women, and >400cells/µl for men	EFV or LPV/r if EFV is contraindicated
EFV	600mg at night (400mg<40kg)	Contraindicated if active psychiatric illness present	NVP or LPV/r if EFV is contraindicated
Lopinavir 200mg / Ritonavir 50mg	2 tabs twice daily (LPV 400mg/r 100mg) 4 tablets twice daily if on TB treatment (rifampicin)	Preferably taken with food For TB patients, increase dose gradually, from 2 BD by taking 3 BD for a week, then 4 BD	Depending on reason for substitution, use ATV/r if available (ATV 300mg/r 100 mg daily)
AZT (Zidovudine)	300mg twice daily	Avoid if severe anaemia (Hb<8g/dL, or <7g/dL in pregnant women)	ABC

7.3 COMMON DRUG TOXICITIES IN PREGNANT WOMEN, ADOLESCENTS AND ADULTS

Fat Redistribution Syndrome (FRS) (lipodystrophy/lipohypertrophy) is common in adolescents adherent to NRTIs such as **Stavudine and Didanosine**. Signs of FRS include loss of subcutaneous fat, facial wasting, truncal adiposity, enlarged breasts and buffalo hump. It is important for clinicians to recognise these debilitating signs as they may contribute to body image problems and are stigmatizing in children and adolescents and can result in poor adherence.

Bone density reduction due to Tenofovir. HIV itself is a risk factor for bone density reduction but studies show an initial increase in bone loss which seems to plateau after about 24 weeks. Current resource constraints do not allow for routine bone density measurements (DEXA scanning), however, any signs of possible osteoporosis (e.g. vertebral, rib, hip, wrists or other fractures not adequately explained by the degree of trauma fractures) warrant investigation.

Renal tubular dysfunction due to Tenofovir. Regular monitoring of creatinine clearance (Cr Cl) and urine dipstix is necessary, particularly if TDF is used with a PI such as Lopinavir/Ritonavir. Urine dipstix should be performed as per monitoring guideline. Proteinuria ≥1+ in the absence of leukocytes/nitrites or glycosuria warrant further investigation including a blood urea, creatinine, calcium/magnesium/phosphate (CMP) and HCO3 and thendiscussion with an expert to determine need for further investigation/referral. Cr Cl should be measured at baseline (prior to ART initiation) 3 months, 6 months, 12 months and yearly thereafter. It is important that Cr Cl tests are actively followed up to ensure results are received as quickly as possible (preferably 1–4 weeks) and that the Cr Cl is calculated using the formula provided above. The automatic calculations of national laboratories are made based on age and gender and do not accurately reflect the Cr Cl of the growing adolescent. Such active follow-up can be beneficial and ultimately, life-saving.

Abacavir*-related hypersensitivity reaction (ABC HSR)*. ABC HSR is uncommon in black African patients but may occur in up to 5% of Caucasian patients. It usually occurs within the first few weeks of initiation and is suspected with the presence of at least 2 symptoms from the following;

including fever, rash, constitutional symptoms, gastrointestinal symptoms and respiratory symptoms. There is a strong association with HLA B5701 typing, rarely investigated locally.

If ABC HSR develops, supportive therapy, usually including hospital admission is required and all ART must be discontinued if the adolescent is unstable, or ABC can be switched if the adolescent is stable. When the adolescent has stabilised, ART can be restarted but ABC must not be included in the regimen as re-exposure is potentially life threatening.

Hyperlipidemia in adolecents with HIV.Hyperlipidemia is challenging to manage in all children and adolescents. The American Academy of Pediatrics criteria for intervention and treatment of persistent pediatric hyperlipidemia suggests using LDL>4.9 mmol/L for children with no known Cardiovascular Disease (CVD) risk factors or LDL >4.1 mmol/L for children with 2 or more CVD risk factors for intervention. HIV as a chronic inflammatory condition may represent a risk factor but is not clearly stated as such.Protease inhibitors and stavudine are associated with increased risk of abnormal lipid profile.

Gynaecomastia and lipomastia. Breast enlargement occurs in both boys and girls usually in the adolescent age group. Efavirenz (EFV)seems to be the offending agent. This could potentially impact on adherence. Changing EFV to another agent may be helpful. In severe cases these patients may require a surgical opinion.

7.3.1 Lactic acidosis in children

All nucleoside analogues have been associated with lactic acidosis. It is a rare but potentially life-threatening metabolic complication of treatment. The pathogenesis is believed to involve drug-induced mitochondrial damage. Initial symptoms are variable; cases have occurred as early as one month and as late as 20 months after starting therapy, and are usually associated with Didanosine or Stavudine.

Note: there are no good screening tests to detect lactic acidosis and a high index of clinical suspicion should be maintained.

CLINICAL FEATURES	**LABORATORY ABNORMALITIES**
• Generalized fatigue, weakness • Gastrointestinal symptoms (nausea, vomiting, diarrhoea, abdominal pain hepatomegaly, anorexia, and/or sudden unexplained weight loss) • Respiratory symptoms (tachypnoea and dyspnoea) • Neurologic symptoms (including motor weakness)	• Hyperlactataemia (>2mmol/L) • Increased anion gap [(Na + K) - (Cl + HCO3); normal <15] • Elevated aminotransferases, CPK, LDH, lipase, and amylase • Micro vesiculars teatosis is seen on histology of the liver
MANAGEMENT • Discuss with a treatment expert • ART should be discontinued in patients with symptoms • Symptoms associated with lactic acidosis may continue or worsen following discontinuation of ART • Therapy is primarily supportive (fluid, bicarbonate administration and respiratory support) • Administration of Riboflavin, Thiamine and/or L-Carnitine has been reported by some to have benefit in case reports	

7.3.2 Abacavir hypersensitivity reaction (HSR)

CLINICAL FEATURES

This is a multi-organ process manifested by signs or symptoms from at least two of the following groups:

- Fever is the most common manifestation occurring in 80% of cases. Chills have been reported to accompany fever
- Rash is experienced by 70% of cases and pruritus can also occur. In contrast to NVP, the rash is often mild and may go unnoticed by patients. When rash occurs in the absence of other features of HSR, Abacavir should not be discontinued
- Gastrointestinal symptoms such as nausea, vomiting, diarrhoea and abdominal pain are all features of HSR but may also occur in the absence of HSR, particularly when Abacavir is used with Zidovudine. Therefore, as with rash, patients with isolated gastrointestinal symptoms should not discontinue Abacavir but should be followed closely
- Constitutional symptoms include fatigue, myalgias and generalized malaise
- Respiratory symptoms occur in 18% of cases and include dyspnoea, cough and pharyngitis. Symptoms may be difficult to distinguish from influenza and other respiratory viruses. Respiratory symptoms together with abdominal symptoms suggest HSR rather than influenza or other respiratory illness. Clusters and combinations of symptoms are important in the diagnosis of Abacavir HSR
- With Abacavir HSR, there is an accentuation of symptoms in the hours immediately after the dose and worsening of symptoms with each subsequent dose. Stopping therapy is followed by rapid improvement in the symptoms
- If Abacavir is not stopped or is restarted after temporary cessation, the HSR will progress to hypotension, renal dysfunction and bronchospasm and ultimately, death. Abnormal laboratory findings may include leukopenia, anaemia and thrombocytopenia, as well as elevations in transaminases, urea, creatinine and LDH. Eosinophilia is usually absent. Patch testing is currently only a research tool
- Resuming with Abacavir may lead to anaphylaxis and should be avoided even in cases where there was diagnostic uncertainty.

MANAGEMENT

On commencement of Abacavir, patients should be counselled in detail about the possible signs of HSR and be advised to contact their care provider should any occur. Therapy should not be initiated in patients with inter-current symptoms to avoid confusion.

It is advisable for patients to discuss symptoms early with the clinician rather than terminating therapy without consultation. Where termination without consultation occurs, Abacavir cannot be reinitiated. Patients should also be made aware of the special “patient alert card” that comes in the packaging. This card should be presented to any healthcare provider who sees the patient especially when care is not given by the usual provider. Providers at emergency facilities may be less familiar with this condition and where possible contact information for the usual care provider should be provided as well.

Deciding whether to stop therapy in a patient with suggestive symptoms can be difficult given the very non-specific nature of the presentation. A detailed medical history should be obtained. The following should be considered:

- When was Abacavir initiated? In the case of Abacavir HSR usually within the past 6 weeks
- Are two or more systems involved?
- Do the symptoms increase with each dose?
- Do the symptom exacerbate just after the dose?

- Do the symptoms fit into the well-recognized clusters?
- What other medications are used and what was the timing of their initiation?

If patients present with mild symptoms and it is not clear whether symptoms are due to HSR, the clinician may consider allowing an additional dose. The patient should be able to report back or else hospitalization may be required for observation. If symptoms worsen, Abacavir should be terminated immediately and permanently. If symptoms do not worsen, Abacavir can be carefully continued while other possible reasons for the patient's symptoms are investigated. In patients where the diagnosis is thought to be clear or where there is sufficient concern, Abacavir should be terminated immediately and permanently.

Hospitalization and special investigation will depend on the severity of symptoms. Corticosteroids do not prevent or alter the natural history. The reaction usually improves within 48 hours.

7.3.3 BCG adverse events

PRESENTATION

Adverse events related to BCG immunization have also been reported during immune reconstitution. These include:

- Abscess at the site of injection 10-15mm
- Lymphadenitis (>1,5cm) (lymphadenopathy may also occur at other sites, e.g. supraclavicular and cervical)
- Suppurative lymphadenopathy in association with BCG injection
- Disseminated BCG disease (indicated by failure to thrive, fever, hepatosplenomegaly)
- Osteitis
- Skin and eye reactions including erythema nodosum, lupus vulgaris and iritis

MANAGEMENT

If these adverse events are noted it is important to notify the authorities on a vaccine adverse event form. If an abscess is present, it should be drained to avoid sinus formation

Pus may be sent for TB culture and PCR for detection of Mycobacterium bovis - BCG should be requested

Most infants with localized BCG reaction will get better without anti-mycobacterial drugs, especially if it is part of an immune reconstitution inflammatory syndrome (IRIS)

Dissemination of BCG disease should be looked for with sputum, abdominal sonar and other investigations as indicated

Only children with disseminated BCG disease should routinely receive treatment with INH (20mg/kg/day), Rifampicin (15 mg/kg/day) and Ethambutol (25 mg/kg) for a period of 6 months. BCG is inherently PZA resistant and the current strain of BCG used in South Africa has low-level resistance to INH, hence the choice of drug regimen

Single TB drugs are usually only available at hospital level and the patients should be referred appropriately

7.4 Common side-effects of drug sensitive TB therapy and ART

Side-effect	ARVs	TB Treatment
Nausea	AZT; PIs	Pyrazinamide
Hepatitis	NVP; EFV; PIs	Pyrazinamide, Rifampicin, INH
Peripheral neuropathy	d4T; ddI	INH
Rash	NVP; EFV	Rifampicin; INH; Pyrazinamide
TB therapy carries significant side effects and attention by the healthcare worker to this is as important as with ART		

7.5 COMMON DRUG TOXICITIES AND SIDE-EFFECTS OF ARV DRUGS

Table 28: Common side-effects of ARV drugs

DRUG	SIDE-EFFECTS	RISK FACTORS	SUGGESTED MANAGEMENT
Abacavir	Hypersensitivity reaction	Presence of HLAB*5701 gene	• If ABC is being used in first-line ART, substitute with TDF or AZT • If ABC is being used in second-line ART, substitute with TDF
Atazanavir/r	Indirect hyperbilirubinaemia (clinical jaundice)	• Underlying hepatic disease • HBV and HCV co-infection • Concomitant use of hepatotoxic drugs	LPV/r or DRV/r. If boosted PIs are contraindicated and NNRTIs have failed in first-line ART, consider integrase inhibitors
	Electrocardiographic abnormalities (PR interval prolongation)	• Pre-existing conduction disease • Concomitant use of other drugs that may prolong the PR interval	
Emtricitabine	Severe skin and hypersensitivity reactions	Unknown	Limited options are available
Zidovudine (AZT)	Anaemia, neutropenia, myopathy, lipoatrophy or lipodystrophy	• Baseline anaemia or neutropenia	If AZT is being used in first-line substitute with TDF or ABC
	Lactic acidosis or severe hepatomegaly with steatosis	• BMI >25 (or body weight>75 kg) • Prolonged exposure to nucleoside analogues	

Lamivudine (3TC)	Headache, dry mouth		AE very rare
(NVP)	Hepatotoxicity	• Underlying hepatic disease • HBV and HCV co-infection • Concomitant use of hepatotoxic drug	NVP. If the person cannot tolerate either NNRTI, use boosted PIs
	• Hypersensitivity reaction, Stevens-Johnson syndrome • Potential risk of neural tube birth defects(very low risk in humans) • Male gynecomastia	Risk factors unknown	
	Convulsions	History of seizures	
Efavirenz (EFV)	Persistent central nervous system toxicity (such as abnormal dreams, depression or mental confusion)	Depression or other mental disorder (previous or at baseline) Daytime dosing	
Tenofovir (TDF)	• Flatulence, nausea, diarrhoea, abdominal discomfort • Asthenia • Acute renal insufficiency, Fanconi syndrome • Chronic renal insufficiency		• Active against hepatitis B but not FDA approved for treatment of hepatitis B. In patients with HIV and hepatitis B co-infection, hepatitis may flare upon discontinuation of Tenofovir • Gastrointestinal symptoms may be worse in lactose-intolerant patients; Tenofovir is formulated with lactose • Adjust dosage for renal insufficiency or failure
Lopinavir/ ritonavir	• Diarrhoea, nausea, vomiting • Dyslipidaemia • Elevations in liver function tests • Taste perversion		• Available in tablets or oral solution. Tablets do not require refrigeration • Oral solution contains 42% alcohol • Avoid combining oral solution with

			Metronidazole or Disulfiram. Alcohol in the oral solution may cause Disulfiram-like reaction
Ritonavir	• Nausea, vomiting, diarrhoea, abdominal pain • Elevations in liver function tests • Fatigue • Circumoral or peripheral numbness • Taste perversion • Hyperuricemia		• Capsules are stable at room temperature for up to 30 days • Avoid combining oral solution with Metronidazole or Disulfiram. Alcohol in the oral solution may cause Disulfiram-like reaction • Has significant interactions with many other medications

8 NUTRITION IN INFANTS AND CHILDREN

HIV infection in children often leads to multiple nutritional deficiencies and general malnutrition. Decreased food intake, impaired absorption and increased nutrient requirements all contribute to this.

HIV infection can impair the nutritional status of infected children from soon after infection. Length/height and weight are reduced in almost all infected children and growth faltering often occurs before opportunistic infections or other symptoms present. Growth failure is indeed a sign of possible undiagnosed HIV infection. HIV causes increased energy requirements in the infected child. This initially results in the wasting of lean body tissue and then of fat mass. Lean body tissue is the total amount of muscle and non-fat tissue in the body. Children with severe growth failure and loss of muscle (lean body tissue) are at an increased risk of mortality. ART improves weight, growth and development of infected children and improves their survival.

Besides weight and length/height, another good indicator of a child's general nutritional status is the mid-upper arm circumference (MUAC).

8.1 INFANT FEEDING: BREASTFEEDING AND FORMULA FEEDING

All pregnant **HIV positive, HIV-negative women or women with unknown HIV status** should receive at least 4 antenatal counselling sessions on infant feeding. At every visit, they should be advised to exclusively breastfeed their infants during the first 6 months of life, with appropriate complementary foods being introduced from 6 months and on expressing breast milk and appropriate storage of expressed breast milk.

Breastfeeding can continue for up to 2 years and beyond in HIV-negative women, or may continue up to 12 months for HIV-positive breastfeeding women**.** Mothers must be counselled about the risks of mixed feeding their infants during their first 6 months of life, as exclusive breastfeeding reduces the risk of HIV transmission and improves child survival.

Pregnant/breastfeeding women must be tested for HIV (Table 1, Section 3.4).

Infants of HIV-positive mothers who are on second or third-line ART for >3 months and have a viral load >1000 should not be breastfed. This is a medical contra-indication to breastfeeding.

They 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 as stipulated in section 6.21 above. Infants who are growth faltering, are at risk of poor growth and should be referred for appropriate nutritional care and support assistance.

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 at public health facilities and be counselled on appropriate exclusive formula feeding in amount and frequency for optimal growth and development. They should be able to provide adequate formula for their infant as a replacement feed to their HIV uninfected infants when specific conditions are met (Box 21).

Box 21: Conditions for replacement infant feeding

- The mother or caregivers able to provide sufficient infant formula to safely exclusively formula feed the infant for the first 6 months of life
- The mother or caregiver can, in the first 6 months, exclusively give adequate infant formula milk
- Safe water and sanitation are assured at the household level and in the community
- The mother or caregiver can prepare infant formula hygienically and correctly
- The mother or caregiver can provide adequate, appropriately constituted formula feeds frequently enough so that it provides adequate nutrition to ensure optimal growth and development of the infant
- Choose a breast milk substitute (commercial infant formula milk product) that is appropriate for the infant's age and circumstances:
    - Infants weighing <2kg should receive a special low birth weight formula until the infant weighs at least 2kg; thereafter infant formula for a full term infant can be given
    - A soy protein-based formula should not be given to an infant <2kg

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.

8.2 ASSESSING THE NUTRITIONAL STATUS OF CHILDREN

The nutritional needs of children who are HIV-positive vary according to age, stage of disease, the presence of acute and/or chronic infections and the treatment they receive. Nutritional needs are best met through a balanced and varied diet in adequate quantities. In the absence of this, additional support may be needed.

Appropriate and adequate nutrition is needed to achieve the full benefits of ART. Children often gain weight and their height increases when ART is initiated, although height gain is generally much slower than weight gain. Monitoring of weight while on treatment is important, as growth failure is often an indicator of treatment failure.

Refer to the South African National Guidelines on Nutrition for People Living with TB, HIV, AIDS and Other Chronic Debilitating Conditions for more information on the nutritional management of children who are HIV-positive.

The ABCDE of nutritional care should be followed when assessing HIV- infected children:

Anthropometry: Plot the child's growth on the relevant growth chart (RTH booklet or clinic chart). Use the chart to assess the child's growth. Classify the child's growth as:

- Normal
- Wasted (weight-for-height <3rd centile)
- Stunted (height-for-age <3rd centile)
- Underweight (weight-for-age <3rd centile)

Biochemistry: These are total cholesterol, serum triglycerides, serum glucose and haemoglobin (Hb)

Clinical: The nutritional needs of children who are HIV-positive for growth, development and immunological function, depend on the stage of disease and history of recent complications such as persistent diarrhoea or opportunistic infections. Children who are HIV-positive have increased

energy needs due to the infection itself, also because children with other opportunistic infections will have even higher requirements.

Dietary: First find out who the child's main caregiver is and who else is involved in feeding and care. This helps to understand the quality and consistency of care practices. Take a brief history of the child's diet to assess the preparation methods, amount and type of food consumed. Children who are HIV-positive often have loss of appetite and opportunistic infections that interfere with the absorption of the nutrients in their food. Questions regarding socio-economic status should be included when talking to the caregiver.

If a child is given infant formula, careful examination of the methods of sterilization of utensils and mixing of the formulas should be performed.

If it is apparent that the child has food insecurity or is not meeting her/his energy requirement, where possible she/he should be referred to a dietician and a social worker to ensure access to child grants and other support.

Evaluation: When a patient has returned for follow-up visits, determine if they were seen by the other health worker(s) they were referred to and assess whether they have improved. Continue to refer until the patient is no longer classified as malnourished or food insecure.

Caregivers should receive appropriate nutritional advice with consideration of cultural and financial constraints. Provide information on food preparation, hygiene, improving energy and nutrient density of meals and give examples of nutritious low cost foods. Adequate nutrition must be established early on as it will help to protect against malnutrition and will improve and maintain the child's growth and quality of life by avoiding infections such as diarrhoea. Preventive measures such as good hygiene, immunisations and regular vitamin A supplements help protect the child against infections and undernourishment.

8.3 Management of severely malnourished children with HIV

The WHO recommends that children that have symptomatic HIV need an additional 30% energy, while symptomatic children with severe malnutrition require up to 100% more energy. It may be difficult to reach an additional 100% of energy requirements, thus the use of nutritional supplement may be required. The **IMCI Chart Booklet (page 22)** provides information on managing feeding problems in infants and young children.

In terms of food supplementation as part of the Integrated Nutrition Programme, the Protein Energy Malnutrition (PEM) Scheme addresses the problem of malnutrition in children. Food supplementation is provided for children whose weight has been monitored on the RTH booklet and is found to be below the 3rd percentile. The programme is administered at primary healthcare facilities.

Parents or caregivers must also be informed about **IMCI feeding recommendations from the IMCI Chart Booklet (pages 20, 21**) and referred to any community support agencies.

Children with severe acute malnutrition (SAM) and any medical complications (or below 6 months of age) must be hospitalized. HIV-positive children with SAM should be managed like all other children with SAM and receive urgent treatment including daily assessment by a doctor. They should be nursed in a high care area until they are feeding well, infections are under control and diarrhoea has stopped. Treatment is aimed at managing the following serious complications: hypoglycaemia, hypothermia, dehydration, electrolyte imbalances, micronutrient deficiencies and infections.

9 HIV AND ANAEMIA

9.1 ANAEMIA IN PREGNANCY

A pregnant woman is deemed to be anaemic when her haemoglobin (Hb) level is below 11g/dl. An Hb <7g/dl is classified as severe anaemia in pregnancy and the women should be referred to a more specialised level of care. Anaemic women have an increased risk of pregnancy complications, including death. If anaemia is corrected, the woman would be able to better withstand the complications of haemorrhage and sepsis. Anaemia is a very common condition, and is more common in women infected with HIV.

9.1.1 Prevention of anaemia in pregnancy

All pregnant women should receive Ferrous sulphate ($FeSO_4$)1 tablet daily and folic acid 5 mg (1 tablet) daily throughout their pregnancy. All women should be given nutritional advice and counselled on the importance of taking their tablets.

9.1.2 Screening for anaemia in pregnancy

- Measure haemoglobin level
  - At first ANC visit
  - At 32 weeks gestational age
  - Near the time of delivery (36 weeks gestational age)
- Look for conjunctival pallor and palmar pallor
- Ask pregnant women at each visit if they get tired easily or get short of breath doing routine tasks

9.1.3 Management of anaemia in pregnancy

Immediate action should be taken if there is anaemia, as summarised in Table 29.

Table 29: Action for anaemia

Hb	Action
If Hb <7g/dl	• Ferrous sulphate ($FeSO_4$) 1 tablet three times a day • Folate 5mg daily • **Urgently refer for obstetrician review**
Hb 7- 10g/dl	• $FeSO_4$ 1 tablet three times daily • Folate 5mg daily • Check Hb again 2 weeks later – if no improvement, **consult with an obstetrician**
Hb >10 - 11g/dl	• $FeSO_4$1 tablet twice a day • Folate 5mg daily • Check Hb again4 weeks later–if no improvement consider referral for obstetrician review or consult with an obstetrician

NOTE: All women should be counselled on the importance of taking their tablets and appropriate nutritional care and support provided.

9.2 ANAEMIA IN INFANTS AND CHILDREN

9.2.1 Common causes of anaemia in infants and children

Anaemia is common in children who are HIV-positive and establishing a cause depends on the clinical features and the ability to investigate and refer infants. Children should be treated for possible common causes and see if they will respond well before referral. Common causes are summarized in Box 22.

Box 22: Common causes of anaemia in HIV-positive children

Anaemia is common in HIV-positive children and may be due to acute illnesses such as:

- Nutritional deficiency
- Opportunistic infections
- Drugs (Cotrimoxazole, Zidovudine and other ARVs)
- Auto-immune haemolysis
- Parvovirus infections
- Direct effects of HIV on bone marrow
- Sickle cell anaemia
- Thalassemia
- Other congenital causes of anaemia may co-exist
- Malaria (less common in South Africa)

Iron deficiency occurs commonly in HIV-positive and HIV-uninfected children. Geohelminths such as *Trichuris trichuria* (whipworm) and *Necator americanus* (hookworm) are prevalent and contribute towards anaemia.

Anaemia is due to iron-deficiency in many cases. A therapeutic trial of iron can be attempted ONCE and only prior to referral for more investigations. It should be preceded by a baseline Hb and REPEATED after 3 weeks to document a response (expected response ≥2g/dL). A base-line reticulocyte count is most useful in differentiating between haemolytic anaemia and marrow suppression.

9.2.2 Treatment for iron deficiency anaemia

Elemental Iron: 2mg/kg 8 hourly with meals for 3 weeks; if Hb increases ≥2g/dL then continue for 3 more weeks)

9.2.3 Dietary management of iron deficiency anaemia

Iron deficiency can be caused by a diet poor in iron rich foods or high consumption of food that prevent the absorption of iron. Caregivers of children should be encouraged to feed their children diets rich in iron. There are two types of iron that are absorbed into the body differently and come from different sources. The first is called haem iron, which is found in meat and meat products. Calcium is the only nutrient to negatively affect the absorption of haem iron. Non-haem iron is found in a variety of foods. The absorption of non-haem iron is affected by the amount of iron the body has in its stores and other nutrients that are eaten with the source of non-haem iron.

9.3 ANAEMIA IN ADOLESCENTS AND ADULTS

Patients should have a full clinical history, an examination, a full FBC, smear and reticulocyte count to characterise the anaemia. Decisions regarding further investigation can be made once this has

been done. AZT may complicate this further, and should be used with care and close monitoring in these patients.

Anaemia pre-ART:

Anaemia is very common in patients with low CD4 counts. Those who are relatively asymptomatic or who have a serious opportunistic infection (OI)like TB, that explains the anaemia, should have their ART started right away and monitored carefully. In other patients, an Hb<8 g/dl with no clear cause should generally trigger additional investigations; usually, there is an underlying serious OI, often TB, and this requires urgent diagnosis and treatment. A low Hb is an independent poor prognostic factor in HIV, so these patients should not delay ART if at all possible.

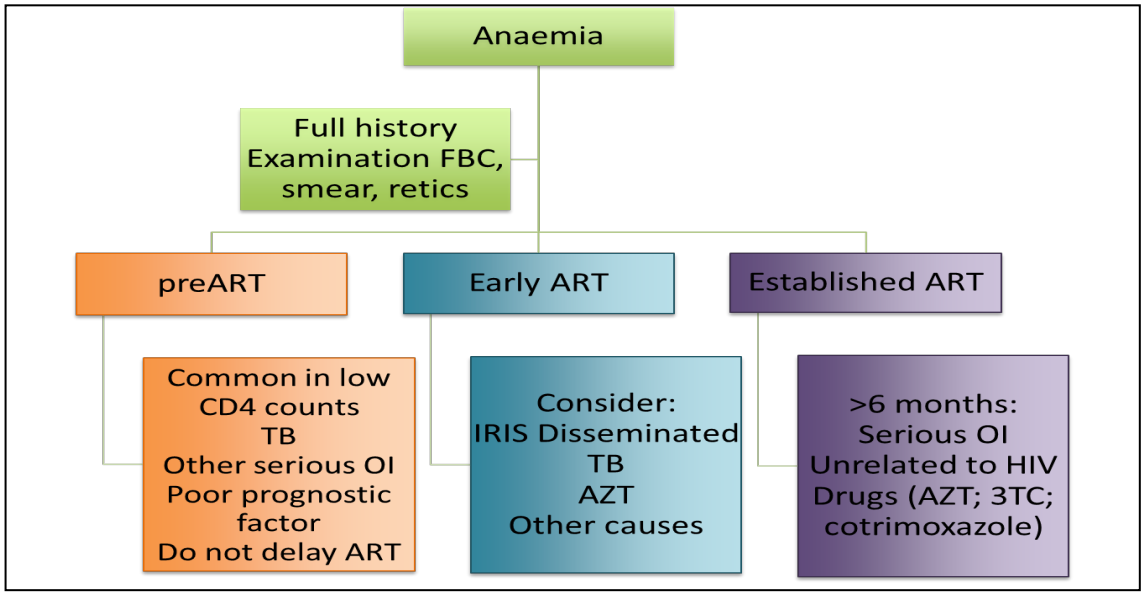
Anaemia immediately after ART initiation:

Confirm that the Hb has dropped, by comparing previous results. Again, a full history, examination and interpretation of an FBC/smear/reticulocyte count are helpful. Common causes of anaemia in the first few weeks and months of treatment include IRIS, disseminated TB, and AZT containing regimens, although many other conditions can cause this.

Anaemia once on established ART (>6 months):

This is unusual and often suggests a serious OI or a condition unrelated to HIV. However, drugs should still be considered as AZT, pure red cell aplasia from 3TC or cotrimoxazole may also cause FBC abnormalities.

Figure 9: Algorithm on anaemia in adults



10 PREVENTION AND MANAGEMENT OF OPPORTUNISTIC INFECTIONS

10.1 ISONIAZID PREVENTIVE THERAPY

10.1.1 Exclusion of active Tuberculosis

It is essential to exclude active TB in every patient prior to starting preventive therapy. This is critical in order to avoid giving a single anti-TB drug to patients who require a full treatment regimen. All people living with HIV should be screened for TB at every visit to a health facility or contact with a health worker. Symptom based TB screening is sufficient to exclude TB among adults and adolescents living with HIV.

TB screening involves asking questions about TB symptoms to identify TB suspects and to find out if the patient may have active TB. This must be done routinely by trained lay counsellors or healthcare workers, as stipulated in Table30and refer or investigate as appropriate.

Table 30: TB symptom screening

TB symptoms screen (adolescents/adults/pregnant women)	TB symptoms screen (infants and children)
Current cough of any duration	Current cough
Persistent fever of more than two weeks	Persistent fever of more than two weeks
Unexplained weight loss of >1.5kg in a month	Poor weight gain
Drenching night sweats	Recent (<12 months) close contact with TB-infected person
	Fatigue

All patients with one or more of these symptoms and signs must be further investigated for active TB disease as per national TB guidelines.

10.1.2 Eligibility for TB preventive therapy

All HIV-positive adults and adolescents with no signs or symptoms suggestive of active TB are eligible for TB preventive therapy.

Table 31: IPT eligibility criteria

POPULATION	Duration of IPT	COMMENT
Pregnant/breastfeeding HIV positive women	• Tuberculin Sensitivity Test (TST) positive: 36 months • TST negative: 12 months • TST not available: 12 months	• All should be on lifelong ART • IPT can be started anytime during pregnancy/breastfeeding • Woman who fall pregnant on IPT should continue IPT • If TST negative, re-assess TST status 1 year after completing IPT
Children <5 years old with recent exposure to TB contact regardless of HIV status	• 6 months	• Recent refers to <12 months • If re-exposed to a TB case after completion of 6 months IPT, repeat another course of IPT irrespective of interval between treatment and
All HIV-positive children		

POPULATION	Duration of IPT	COMMENT
up to 15 years old with recent exposure to TB case		re-exposure • If child is exposed to new infectious source while on IPT, continue IPT for as long as source remains infectious
Pre-ART patients regardless of CD4 (Adolescent/Adult)	• TST positive: 36 months • TST negative: No IPT • TST not available: 6 months • If later TST becomes negative – stop IPT • If later TST becomes positive – extend to 36 months	• Must be TST positive to get IPT regardless of CD4 • If TST negative, re-assess TST status annually in Pre-ART • IPT can be started anytime • If patient becomes eligible for ART while on IPT, initiate ART and do not stop IPT • If eligible for both ART and IPT, start with ART, followed by IPT when stable on ART
Patients on ART (Adolescent/Adult)	• TST positive: 36 months • TST negative: 12 months • TST not available: 6 months • If later TST becomes positive – extend IPT to 36 months	• All eligible for IPT regardless of CD4 count • If TST negative, re-assess TST status and IPT eligibility 1 year after completing IPT
Former TB adult patients (Excluding MDR/XDR and children)		• There must be documented proof of bacteriological cure • If there is no proof of cure, do not give IPT, re-assess for IPT eligibility after 3 months • Can be started immediately after completing TB treatment
NOTE: If TST is not initially available at initiation of IPT, it must be done within ONE month of initiating IPT. If TST is negative, re-assess TST status annually until it becomes positive		

There is currently no evidence for repeating IPT in those who have completed 36 months or extending IPT beyond 36 months.

Individuals suspected of having TB should be investigated and if it is not found, they should not be given IPT. They should be re-assessed for IPT eligibility after 3 months.

10.1.3 Treatment and Dosing guide for INH for children, adolescents and adult

Table 32: Dosing guide for standard regimen for TB preventive therapy

Adolescents/Adults/Pregnant women	Children
Isoniazid (INH): 5 mg/kg/day (maximum 300 mg per day) Vitamin B6 (pyridoxine): 25 mg/day Vitamin B6 given with INH to prevent	INH 10 mg/kg/day Crush appropriate fraction of the 100mg INH tablet and dissolve in water or multi-vitamin syrup before giving it to the child HIV-positive or malnourished, add Pyridoxine daily

Adolescents/Adults/Pregnant women	Children
peripheral neuropathy Issue 1-month drug supply for 3 months, thereafter a 3-month supply can be issued	for 6 months at the following dosages: • <5 years of age: 12.5mg daily • >5 years of age: 25mg daily

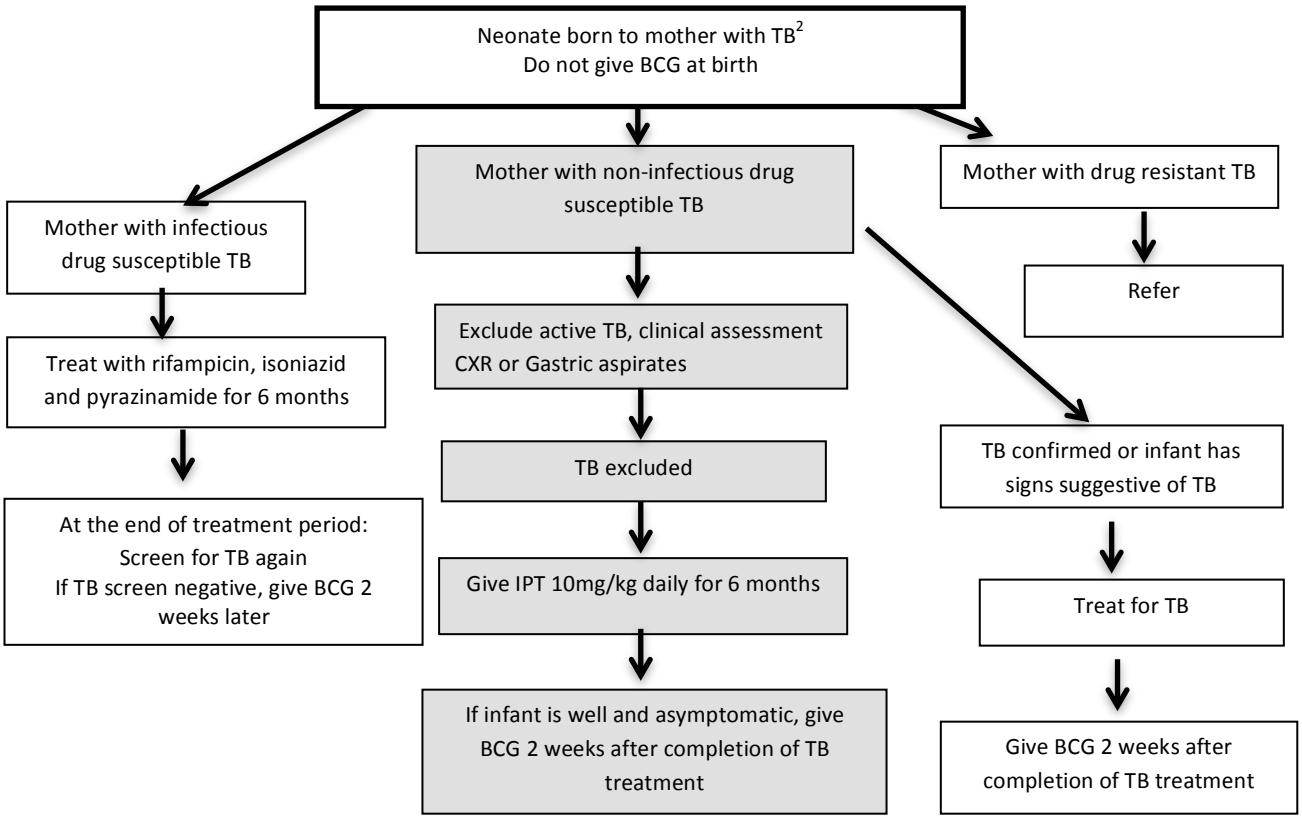
10.1.4 Infants born to mothers with TB

The following neonates are eligible for IPT:

- If TB has been excluded on basis of clinical, radiological (CXR) and bacteriological (gastric aspirates) assessments and
- Mother is non-infectious and has drug susceptible TB

If eligible, prescribe INH 10mg/kg daily for 6 months.

Figure 10: Management of infants born to mothers with TB



10.1.5 Who is not eligible for TB Isoniazid Preventive Therapy?

- People with confirmed or unconfirmed active TB
- Patients with active liver disease (acute or chronic)
- Patients with symptoms of peripheral neuropathy
- Patients with a history of adverse reaction to Isoniazid
- People who are HIV positive but TST negative in pre-ART care
- Patients with excessive alcohol use; more than 28 units per week for men and 21 units per week for women
- People who have completed treatment of MDR- or XDR-TB

- Patients who are ill and/or are in unstable condition

10.1.6 Isoniazid side-effects and management

Side-effect	Management
Peripheral neuropathy	• Increase vitamin B6 (pyridoxine) to 100 mg daily; keep patient on that dose until the symptoms disappear • If peripheral neuropathy is severe, discontinue INH immediately and refer patient to hospital • If patient needs to take d4T for medical indication, discontinue INH
Hepatotoxicity	• Stop INH immediately and refer patient to hospital
GI effects	• Rule out other causes of nausea and vomiting • Consider LFTs • Treat symptomatically (if no other cause is found)
Flushing reaction	• Reassure patients and advise that they avoid tyramine and histamine-containing foods while on INH • Flushing is usually mild and resolves without therapy
Hypersensitivity	• Discontinue until the reaction resolves • Re-challenge after resolution of reaction • Begin with INH 50mg on day 1 • If the original reaction was severe, begin with INH 5mg on day 1 • If a reaction does not occur after day 1 dose, increase to 300mg on day 2 • If a reaction does not occur after the day 2 dose, continue INH 300mg daily • If a reaction occurs during drug re-challenge, stop INH • Treat with antihistamines and follow-up

10.2 COTRIMOXAZOLE PREVENTIVE THERAPY

10.2.1 Cotrimoxazole prophylaxis in infants, children and early adolescents

Refer to Section 6.2.2

10.2.2 Cotrimoxazole prophylaxis in late adolescents and adults

Cotrimoxazole prophylaxis markedly reduces hospitalization and mortality and provides protection against *Pneumocystis Jiroveci* pneumonia (PCP), toxoplasmosis, malaria and many other bacterial infections.

Table 33: Eligibility criteria for Cotrimoxazole prophylaxis

Children	Adolescents and Adults
• HIV-exposed infants <1 year, start CTP at 4-6 weeks age • HIV-positive infants < 1 year • HIV-positive children 1-5 years with WHO stage 2,3,4, CD4<25% or <500 • HIV-positive>6years with WHO stage 3,4 • TB/HIV co-infection • Any child at risk of malaria or any bacterial infection	• Patients with CD4 ≤200 cells/µl • WHO stage 3 or 4 • HIV/TB co-infection

- Cotrimoxazole is safe to use in pregnancy. Pregnant women must continue on CPT
- CPT should be taken until CD4 rises above 200cells/µl in adults for at least 6 months
- Prescribe 160/800 (2 single strength tablets) orally once daily
- Monitor patient clinically at 3 monthly interval
- Do not delay ART in favour of cotrimoxazole initiation. Ideally, initiate cotrimoxazole immediately at first adherence visit, if not done already, prior to ART
- Cotrimoxazole's most common side effect is a maculopapular rash. Prophylaxis may be continued in the presence of mild rash or interrupted and then reintroduced. Treatment should not be continued in the presence of fever, hepatitis or mucous membrane lesions e.g. Stevens-Johnson syndrome
- Neutropenia is a rare side effect of CPT – routine blood count monitoring is not necessary
- Use Dapsone 100 mg a day for patients who have had a mild reaction to cotrimoxazole. Dapsone should not be used after severe reactions, as there may be cross-reactivity. Dapsone does not provide protection against bacterial infections and provides only limited protection against toxoplasmosis
- Stop CPT only once well on ART and CD4 >200cells/µl on more than two occasions
- Recommence cotrimoxazole when CD4 drops below 200cells/µl or if ART fails or a new opportunistic infection develops

10.3 CRYPTOCOCCUS (CRYPTO) SCREENING AND TREATMENT

Cryptococcus is found in soil from bird droppings that are breathed in as dust. It cannot be passed in the air from one infected person to another. Infection can be dormant for many years.

Cryptococcus is only a problem if CD4 count drops to below 100 cells/µl. Smokers and people who work outdoors have higher risk of Cryptococcus.

10.3.1 Screening for cryptococcal disease in adults

- HIV-positive adults with a CD4 count <100 cells/µl should be screened for cryptococcal disease *before* ART is started
- Screen for cryptococcal antigenaemia by reflex laboratory/ clinician-initiated testing
- Patients with a prior diagnosis of cryptococcal meningitis do not need to be screened
- Patients with a positive cryptococcal antigen (CrAg) blood test have disseminated cryptococcal disease and should be *specifically* evaluated for symptoms/ signs of meningitis
- CrAg-positive patients with symptoms/signs should be referred for lumbar puncture (LP) to exclude cryptococcal meningitis. If cryptococcal meningitis is confirmed on LP, patients should be managed in hospital (for at least 2 weeks) and ART deferred for 4-6 weeks
- CrAg-positive patients without symptoms/signs may be offered an LP, if this is immediately accessible, to exclude subclinical meningitis. For CrAg-positive patients without suspected meningitis, oral fluconazole (800 mg for 2 weeks, followed by standard consolidation and

maintenance treatment) is recommended as well as for patients with an LP that is cryptococcal test-negative. For patients without signs or evidence of meningitis, ART is recommended to be started 2 weeks after anti-fungal therapy is initiated

- **Pregnancy**: Women of childbearing age who screen CrAg-positive should have a pregnancy test prior to starting fluconazole (teratogenic); those who are not pregnant and are started on fluconazole should be advised to avoid pregnancy during treatment. CrAg-positive patients who are pregnant should be offered an LP and discussed with an expert before a decision is made regarding management
- **Liver disease**: Patients with evidence of clinical liver disease deserve careful monitoring because fluconazole may cause liver injury

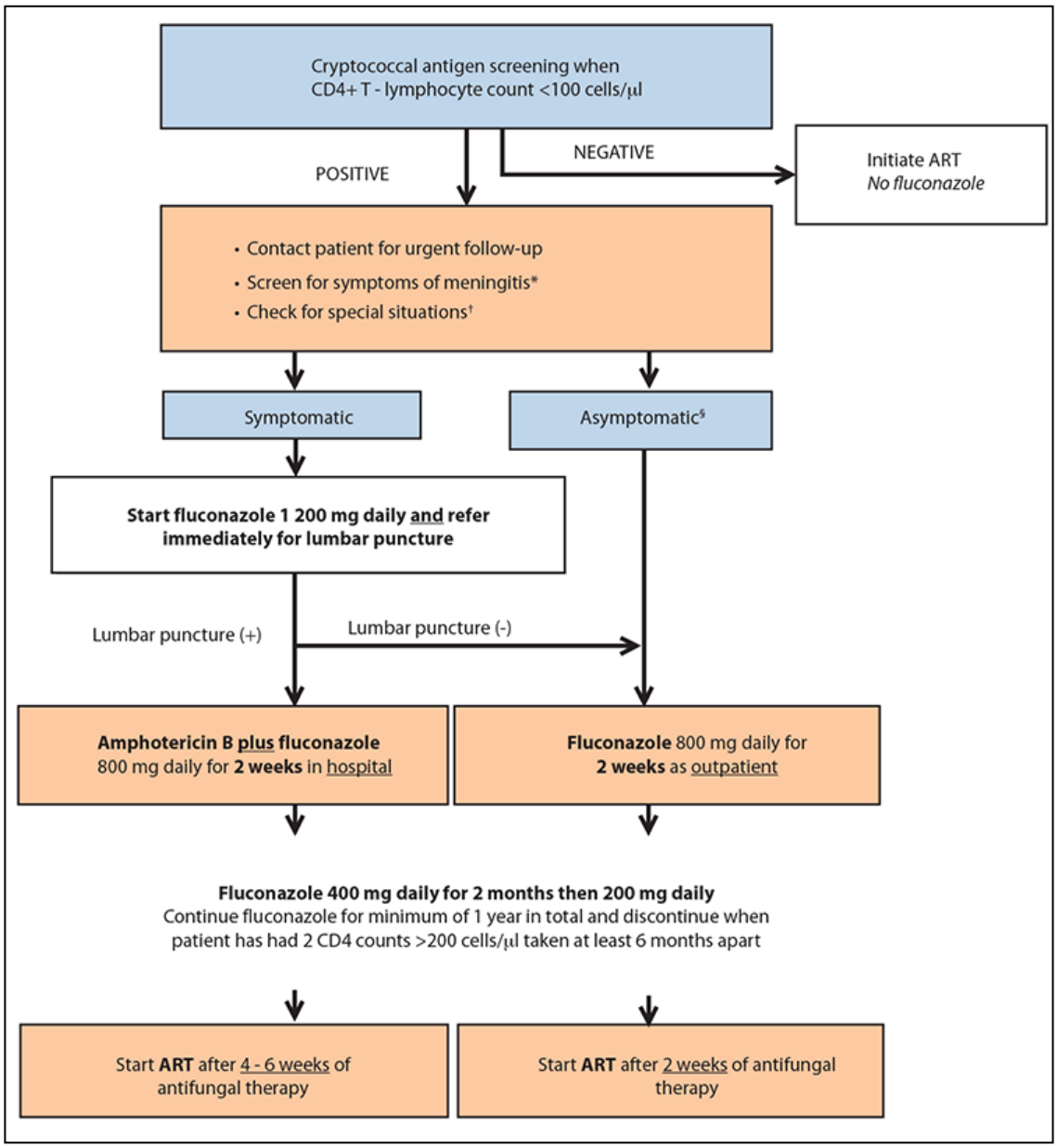
10.3.2 Recommended cryptococcal prophylaxis

Table 34: Cryptococcal prophylaxis

Screening	Antifungal prophylactic treatment	ART
CrAg Screening test positive (bloodstream disease) but no evidence of meningitis	Oral fluconazole (800 mg per day) for 2 weeks, followed by standard consolidation and maintenance antifungal treatment)	Start after 2 weeks of antifungal treatment
Screening test positive with evidence of meningitis	Intravenous antifungal treatment for 2 weeks, followed by standard consolidation and maintenance antifungal treatment	Start after 4-6 weeks of antifungal treatment

10.3.3 Cryptococcal screening and prophylaxis

Figure 11: Algorithm for cryptococcal screening and prophylaxis



10.4 TUBERCULOSIS

HIV-positive patients are at higher risk of developing TB compared to the general population, especially during the period immediately after initiating ART, thereforeall HIV-positive patients should be screened for TB. If an HIV-positive patient has symptoms suggestive of TB, investigate appropriately using sputum/GeneXpert and TB culture as per guidelines. It is very important to investigate patients for TB before starting ART and to routinely screen patients on ART. The guidelines remain the same for pregnant women.

10.4.1 Diagnosis of TB

Suspect TB if one or more of the following are present:

1. Cough over any duration
2. Sputum production which may occasionally be blood stained

3. Fever
4. Drenching night sweats
5. Unexplained weight loss
6. Loss of appetite, malaise, tiredness
7. Shortness of breath, chest pains
8. New palpable lymphadenopathy

In children the presence of any three or more of the following features is suggestive of TB:

- TB symptoms (cough, fever, failure to thrive, weight loss)
- Physical signs suggestive of TB
- Positive TST
- Chest x-ray findings suggestive of TB

10.4.2 TB treatment in HIV

Table 35: ART for adults with concomitant TB

TB develops while on ART	TB diagnosed before starting ART
Continue ARV therapy throughout TB treatment First-line regimen: Patient can remain on the regimen they are taking Second-line regimen: The Lopinavir/Ritonavir dose should be doubled (from 2 tablets 12 hourly to 4 tablets 12 hourly) while the patient is on Rifampicin-based TB treatment Monitor ALT monthly Reduce Lopinavir/Ritonavir to standard dose 2 weeks after TB treatment is completed	In TB/HIV co-infection not on ART Start with TB treatment first, followed by ART as soon as possible and within 8 weeks If CD4 <50 cells/µl initiate ART within 2 weeks of starting TB treatment, when the patient's symptoms are improving and TB treatment is tolerated If CD4 >50 cells/µl initiate ART within 2-8 weeks of starting TB treatment First line ART regimen: • Tenofovir 300mg daily • Lamivudine 300mg daily • Efavirenz 600mg at night

NOTE: HIV positive TB patients qualify for lifelong ART regardless of CD4 cell count.

Complete 2 to 8 weeks maximum, of TB therapy before commencing ART (**and as soon as possible if CD4 count is less than 50 cells/**µl). In general, ART should be initiated as soon as the patient is tolerating their TB therapy; this is usually within 2-4 weeks.

EFV-based regimens are generally preferred in patients with active TB; however, other regimens are also effective. Dose adjustment of PI may be required. Patients on Lopinavir/Ritonavir should have their dose doubled slowly over two weeks (to 800/200 mg twice a day); all other regimens can be continued unmodified. Monitor and investigate appropriately for hepatotoxicity symptoms. Continue these changes to Lopinavir/Ritonavir until two weeks after completion of TB treatment.

Patient developing TB while on ART:

ART should be continued throughout TB treatment.

Cotrimoxazole can cause erythema multiforme and Stevens-Johnson syndrome. If this occurs, stop the Cotrimoxazole.

Dapsone should be used in Cotrimoxazole intolerant patients. The recommended dose is 2 mg/kg/day or 4 mg/kg/week. The maximum daily dose is 100 mg (1 tablet).

11 MONITORING AND EVALUATION

11.1 PURPOSE

The purpose of the monitoring and evaluation section is to:

- Strengthen monitoring and evaluation of the ART programme
- Provide monitoring and evaluation guidance to the consolidated ART guidelines

Monitoring and evaluation activities allow health facilities, the health department at national, provincial and district level, and their partners to assess the extent to which ART programme is being implemented and achieving the intended objectives. Planned and systematic data gathering, analysis and interpretation are essential for the purpose of:

- Monitoring clinical care
- Patient outcome improvement
- Logistical appropriateness
- Program cost-effectiveness
- Performance measures and improvement
- Monitoring effectiveness and quality of services

Monitoring is a continuous function that uses the systematic collection of data on specified indicators to provide management and the main stakeholders of an ongoing development intervention with indications of the extent of progress and achievement of objectives and progress in the use of allocated funds (World Bank, 2009:2).

Evaluation is the systematic and objective assessment of an ongoing or completed project, program or policy including its design implementation and results (World Bank, 2009:2).

11.2 DATA COLLECTION TOOLS

To facilitate a standardised and systematic monitoring, it is compulsory for ART (including paediatric and antenatal care) service points to utilise the approved monitoring data collection tools. Clinicians treating patients should ensure that all required data collection tools are completed in detail. The following tools should be used to collect ART related data:

- **Patient-held card:** The patient-held card should be completed at every visit by the attending clinician and to be given to the patient
- **Maternity case record:** Medical record used by the clinicians for recording the antenatal clinic visits for the duration of the pregnancy including labour and delivery
- **RTH booklet:** The RTH booklet is a record of immunisations and growth rate given to mothers when their infant is born and is used to monitor the development of the child until he/she is five years old
- **HIV and ART clinical stationery:** HIV and ART clinical stationery is a legal record designed for the treatment and care of ART patients in PHC context. The stationery is used to record details of treatment and should be completed in detail at every clinic visit by the treating clinician. This record is facility-based. After every patients visit, information from the clinical stationery is then transcribed into TIER.Net system or ART register
- **ANC register:** A register that chronicles the ANC visits for the duration of the pregnancy
- **Postnatal register:** A register that is used to document the postnatal services received by mother and newborn pair within three days and subsequent visits
- **Well-baby register:** A register that is used to document the baby clinic visits

- **PHC register:** This register may supersede other registers once rationalisation process is finalised
- **Pre-ART register:** Information of all persons who are HIV positive and registered for HIV care (not necessarily receiving ART) is recorded in this register. Once the person is initiated on ART, s/he is registered in the ART enrolment register and followed there. The purpose of registers in general is to collect the same information about an entire group of patients in one location. This allows you to monitor what is happening with your whole group of patients in HIV care, and provides information about starting ART at your facility
- **ART register (3 Tier systems):** The ART register is a tool designed to monitor patients once they have started on ARVs. Once patients are initiated on ART, relevant information from the pre-ART register is transferred to the ART register. Thereafter, only the ART register is used to track these patients (even if the patient subsequently stops ART)
- For Tier 1 facilities, information from the register is collated manually and reported monthly. For patient monitoring and programme monitoring reasons, the purpose of the ART register is to collect the information about groups of patients (**cohorts or ART start-up groups**) who start ART at the same time. For Tier 2 (phase 6) information from the paper-based ART register is transcribed ideally by data capturers into electronic TIER.Net. Data is produced at facility level generated by aggregating individual patient outcomes and exported into the district health information system (DHIS) using data exchange between TIER.Net and DHIS. Data is reported quarterly and, similar to the TB programme, is reported one quarter in arrears
- **Birth register:** A register used to in labour units to document labour and birth data elements
- **Adverse drug reaction reporting form:** A form used to report any untoward reaction to the prescribed drug
- **District health information system:** A routine system for tracking health service delivery in the public health sector. It also plays a pivotal role in the collection, capturing, storage, collation, analysis and reporting of routine data

11.3 DATA TRANSMISSION, ANALYSIS, REPORTING AND USAGE

The responsibility for data collection, analysis, management, reporting and usage rests at four levels (facility/hospital, sub-district/district, province and national). The process of data management involves:

- Clinical documentation by clinicians and pharmacists
- Service provision capturing in register
- Data entry by data capturer
- Data aggregation/collation
- Data analysis
- Reporting by program coordinator (paper or electronic based)
- Data usage

11.4 ROLES AND RESPONSIBILITIES

ART (including paediatric and antenatal care) service points: Data generation, improvement of data quality, data analysis, maintenance of patient records and registers, reporting to the sub-district or district Department of Health and using the information in patient management, drug stocking and referral. Facilities are also encouraged to play specific role in reducing patients' loss to follow-up.

Loss to follow-up (LTFU) tracing

Loss to follow-up is a pervasive challenge noted throughout the country. A loss to follow-up report can be generated through TIER.Net. Data capturers are advised to extract the early and late

missed appointment in Tier 2 facilities for sharing with facility and ART (including PMTCT and paediatric) staff to ensure follow-up.

Table 36: Loss to follow-up tracing: report and action required

REPORT	WHEN TO GENERATE	CONTENT	WHO EXTRACTS REPORT AND ACTION NEEDED
Early missed appointment (2 weeks ago)	Every Friday morning	List of patients needing to be called/visited at home to prevent LTFU	Data clerk to draw each patient folder and confirm missed appointment. Report then to be submitted to facility manager (FM). FM to sign off on list. FM to assign staff member (suggest counsellor) to call each patient and encourage him or her to return. Result of each call to be recorded on list. List to go back to FM for filing
Late missed appointments (2 months ago)	1st Friday of every month	List of patients who need a home visit to stop potential LTF	Data clerk to draw each patient folder and confirm missed appointment. The necessary information should be pulled from patient folders to fill in Community Based (CBS) registers. CBS register and report then to be submitted to FM. FM to sign off on list and report. FM to assign staff member to call each patient or conduct a home visit. Result to be written on report and given back to data clerk. Data clerk to manually enter LTFU for all patients with incorrect address/phone numbers or for those patients not willing to return to facility. Transfer Out (TFO)and name of new facility should be manually entered if the patient is receiving treatment at another facility and the name of the facility is known. Report to be filed in FM office.
Defaulter report	1st Friday of every month	List of patients absent or not having drugs in hand for 90 days or more. NOTE: Patients already captured as LTFU will not be on this list	Data clerk to draw each patient folder and confirm missed appointment. Report then to be submitted to FM. FM to sign off on report and give back to data clerk for entry of LTFU for all patients remaining on list. Once completed, list to be filed in FM office.

Sub-district, District and Provincial Department of Health: Data analysis, quality audit, assessment of ART (including paediatric and antenatal care) service points, supervision, feedback and dissemination of information to National office and stakeholders.

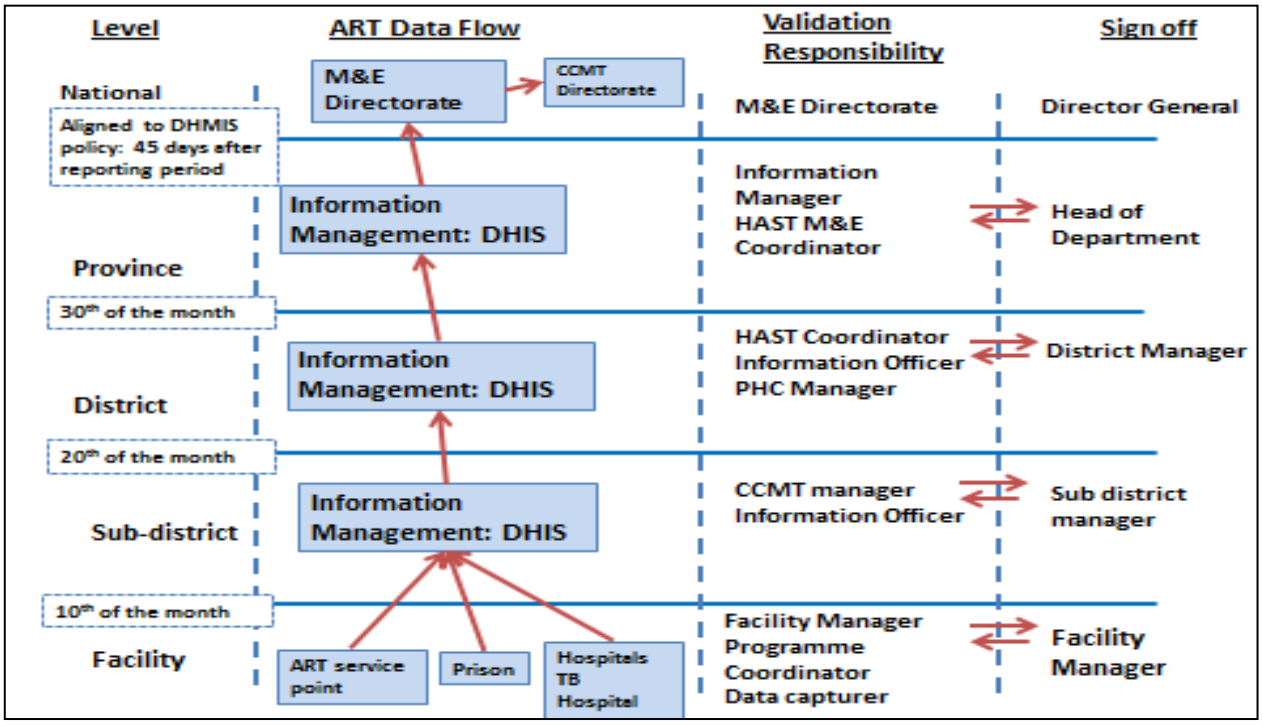
National Department of Health: Compilation, analysis, quality audit, monitoring and evaluation, planning, advocacy resource allocation, drug supply and dissemination of information to national and international stakeholders.

11.5 REPORTING

Reports required by different organisations will be passed up the national monitoring and evaluation reporting channels. Note that reporting is bi-directional. Monitoring and evaluation data, whether analysed or raw must be utilised and reported to the section responsible for corrective action. The principles of ***continuous quality improvement*** dictate that monitoring and evaluation data are not be used punitively nor accessed for anything else, including the courts, other than for performance and quality of care improvement action.

Information from the prescribed records and registers is compiled and used to populate various monitoring reports, which are forwarded to the Sub-district, District and National Departments of Health. Monthly and quarterly reports should be forwarded to the next level of reporting according to the district health management information system (DHMIS) policy. Below is data flow diagram for ART.

Figure 12: Data flow diagram for the ART programme



Reports to be submitted

The reports that should be submitted are monthly/quarterly ART/PMTCT and cohort analysis reports. The data elements collected in various facilities are important in better understanding of cascade of care. The cascade of care and relevant indicators is presented on the next page.

Figure 13: Cascade of care

12 ANNEXURES

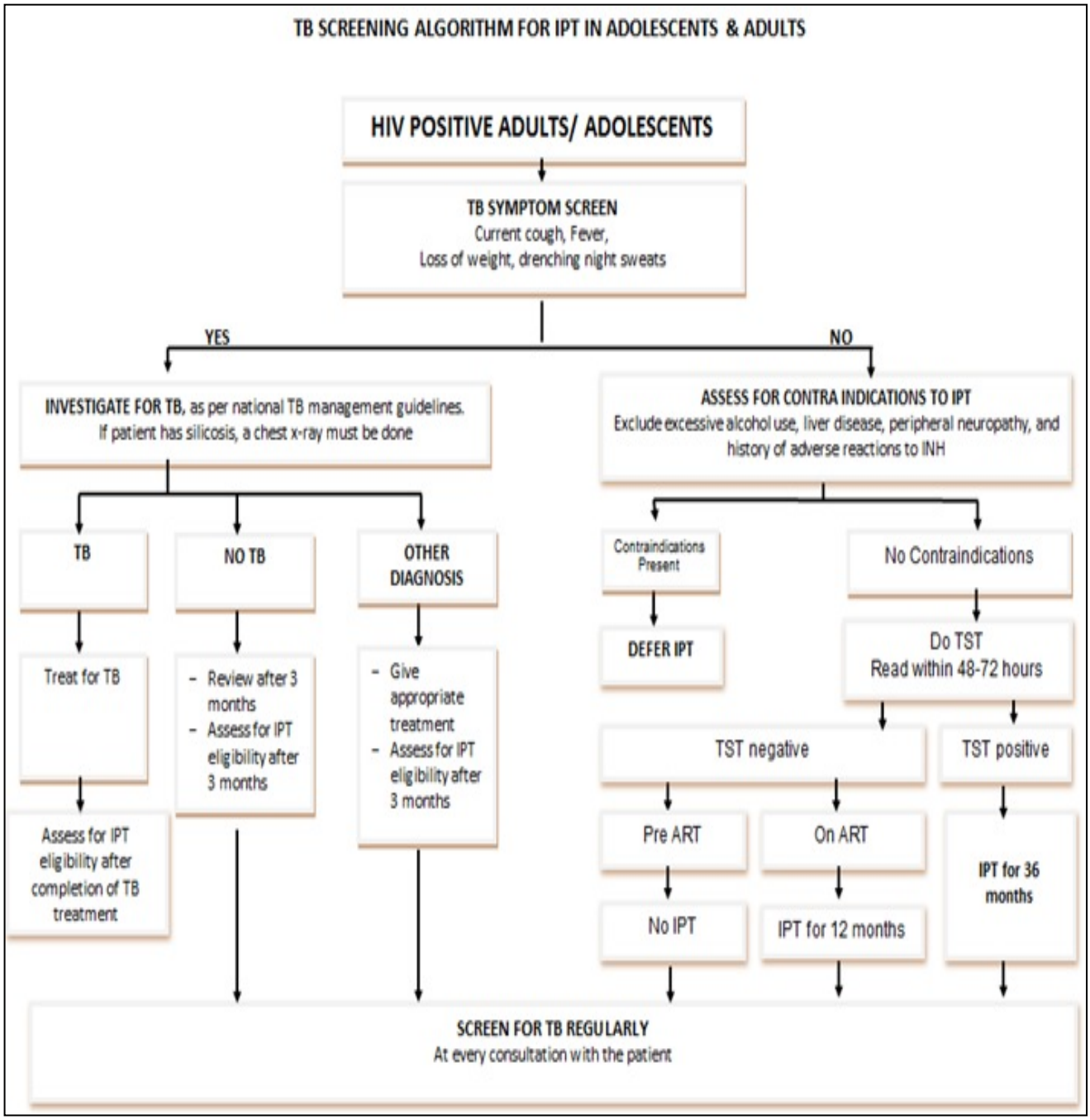
12.1 ANNEXURE 1: WHO CLINICAL STAGING OF HIV/AIDS FOR CHILDREN, ADOLESCENTS AND ADULTS

CLINICAL STAGE	CLINICAL CONDITIONS OR SYMPTOMS (Adolescents and Adults)	CLINICAL CONDITIONS OR SYMPTOMS (Children)
Primary HIV infection	• Asymptomatic • Acute retroviral syndrome	
Clinical stage 1	• Asymptomatic • Persistent generalized lymphadenopathy	• Asymptomatic • Persistent generalized lymphadenopathy
Clinical stage 2	• Moderate unexplained weight loss (<10% of presumed or measured body weight) • Recurrent respiratory infections (sinusitis, tonsillitis, otitis media, and pharyngitis) • Herpes zoster • Angular cheilitis • Recurrent oral ulceration • Papular pruritic eruptions • Seborrheic dermatitis • Fungal nail infections	• Unexplained persistent weight loss • Hepatosplenomegaly • Papular pruritic eruptions • Extensive wart virus infection • Extensive molluscum contagiosum • Fungal nail infections • Recurrent oral ulcerations • Unexplained persistent parotid enlargement • Lineal gingival erythema • Herpes zoster • Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis or tonsillitis)
Clinical stage 3	• Unexplained severe weight loss (>10% of presumed or measured body weight) • Unexplained chronic diarrhoea for >1 month • Unexplained persistent fever for >1 month (>37.6°C, intermittent or constant) • Persistent oral candidiasis (thrush) • Oral hairy leukoplakia • Pulmonary tuberculosis (current) • Severe presumed bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia) • Acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis • Unexplained anaemia	• Unexplained moderate malnutrition not adequately responding to standard therapy • Unexplained persistent diarrhoea (14 days or more) • Unexplained persistent fever (above 37.5°C intermittent or constant for longer than one month) • Persistent oral candidiasis (after first 6-8 weeks of life) • Oral hairy leukoplakia • Acute necrotizing ulcerative gingivitis or periodontitis • Lymph node tuberculosis • Pulmonary tuberculosis • Severe recurrent bacterial pneumonia • Symptomatic lymphoid interstitial pneumonitis • Chronic HIV-associated lung disease including bronchiectasis

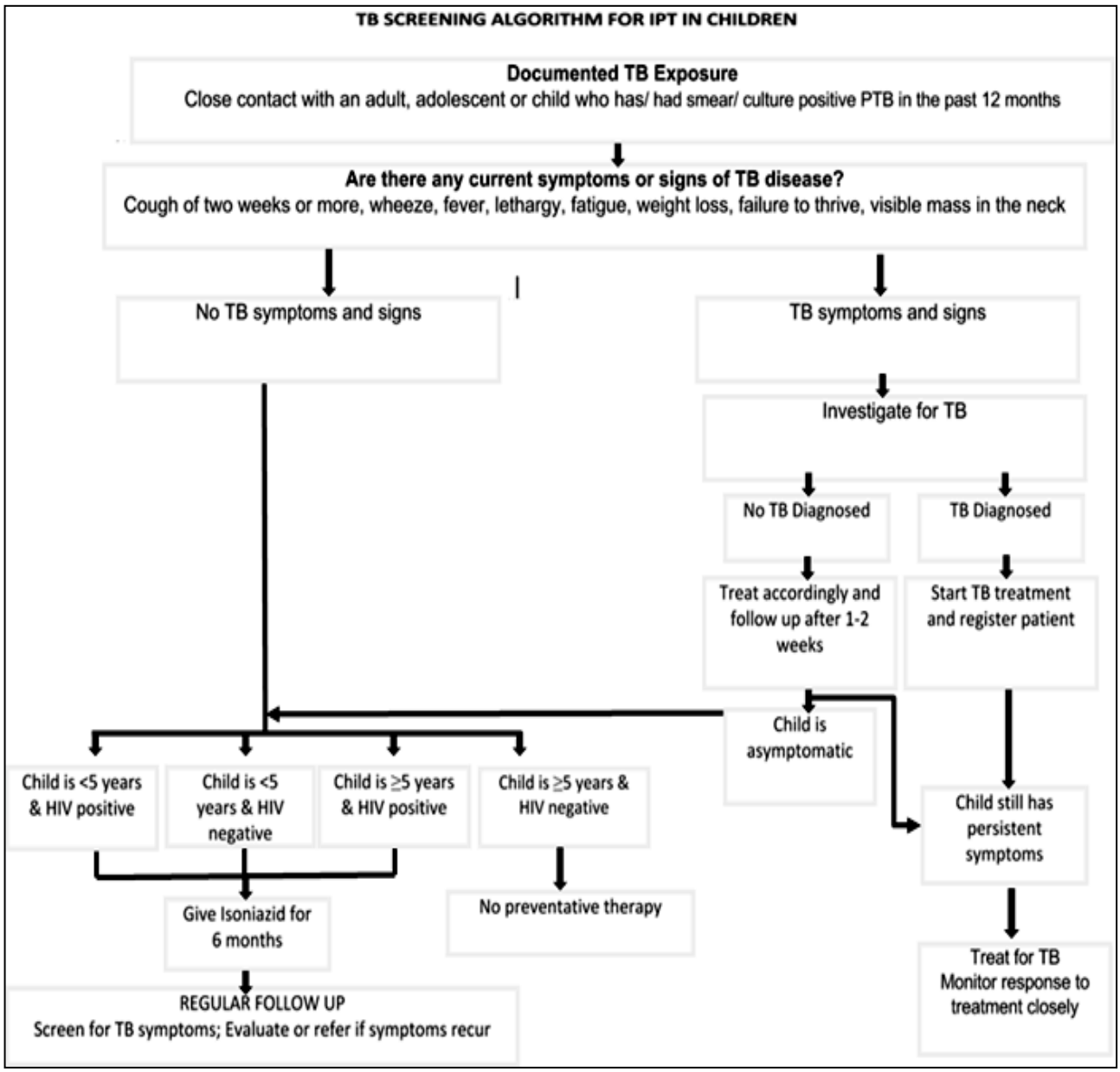
CLINICAL STAGE	CLINICAL CONDITIONS OR SYMPTOMS (Adolescents and Adults)	CLINICAL CONDITIONS OR SYMPTOMS (Children)
	(haemoglobin<8 g/dL) • Neutropenia (neutrophils <500 cells/μL) • Chronic thrombocytopenia (platelets <50,000 cells/μL)	• Unexplained anaemia (<8 g/dL), neutropenia (< 0.5 × 109 per litre) • And/or chronic thrombocytopenia (<50 × 109 per litre)
Clinical stage 4	• HIV wasting syndrome, as defined by the CDC (see Table 1, above) • Pneumocystis pneumonia • Recurrent severe bacterial pneumonia • Chronic herpes simplex infection (orolabial, genital, or anorectal site for >1 month orvisceral herpes at any site) • Oesophageal candidiasis (or candidiasis of trachea, bronchi, or lungs) • Extra pulmonary tuberculosis • Kaposi sarcoma • Cytomegalovirus infection (retinitis or infection of other organs) • Central nervous system toxoplasmosis • HIV encephalopathy • Cryptococcosis, extra pulmonary (including meningitis) • Disseminated non-Tuberculosis mycobacteria infection • Progressive multifocal leukoencephalopathy • Candida of the trachea, bronchi, or lungs • Chronic cryptosporidiosis (with diarrhoea) • Chronic isosporiasis • Disseminated mycosis (e.g., histoplasmosis, coccidioidomycosis, penicilliosis) • Recurrent non-typhoidal Salmonella bacteraemia • Lymphoma (cerebral or B-cell non-Hodgkin) • Invasive cervical carcinoma • Atypical disseminated leishmaniasis • Symptomatic HIV-associated nephropathy • Symptomatic HIV-associated cardiomyopathy • Reactivation of American	• Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy • Pneumocystis pneumonia • Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection or meningitis but excluding pneumonia) • Chronic herpes simplex infection (orolabial or cutaneous of more than one month's duration or visceral at any site) • Extra pulmonary tuberculosis • Kaposi sarcoma • Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) • Central nervous system toxoplasmosis (after one month of life) • HIV encephalopathy • Cytomegalovirus infection: retinitis or cytomegalovirus infection affecting another organ, with onset at age older than one month • Extra pulmonary cryptococcosis (including meningitis) • Disseminated endemic mycosis (extra pulmonary histoplasmosis, coccidiomycosis) • Chronic cryptosporidiosis • Chronic isosporiasis • Disseminated non-tuberculous mycobacterial infection • Cerebral or B-cell non-Hodgkin lymphoma • Progressive multifocal leukoencephalopathy • Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy • HIV-associated rectovaginal fistula

CLINICAL STAGE	CLINICAL CONDITIONS OR SYMPTOMS (Adolescents and Adults)	CLINICAL CONDITIONS OR SYMPTOMS (Children)
	trypanosomiasis (meningoencephalitis or myocarditis)	

12.2 ANNEXURE 2: TB SCREENING ALGORITHM FOR IPT IN ADOLESCENTS AND ADULTS

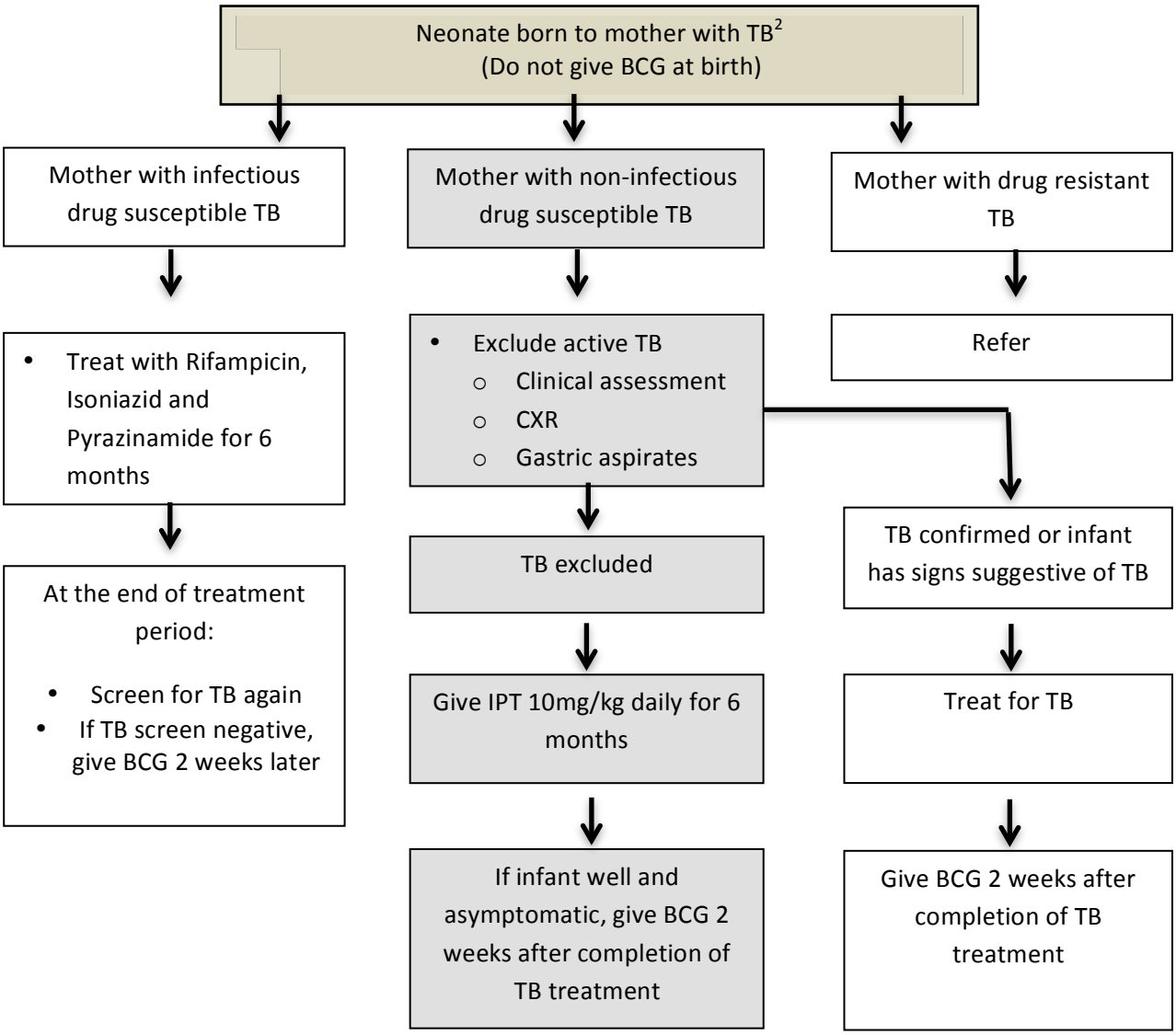


12.3 ANNEXURE 3: TB SCREENING ALGORITHMS FOR IPT IN CHILDREN

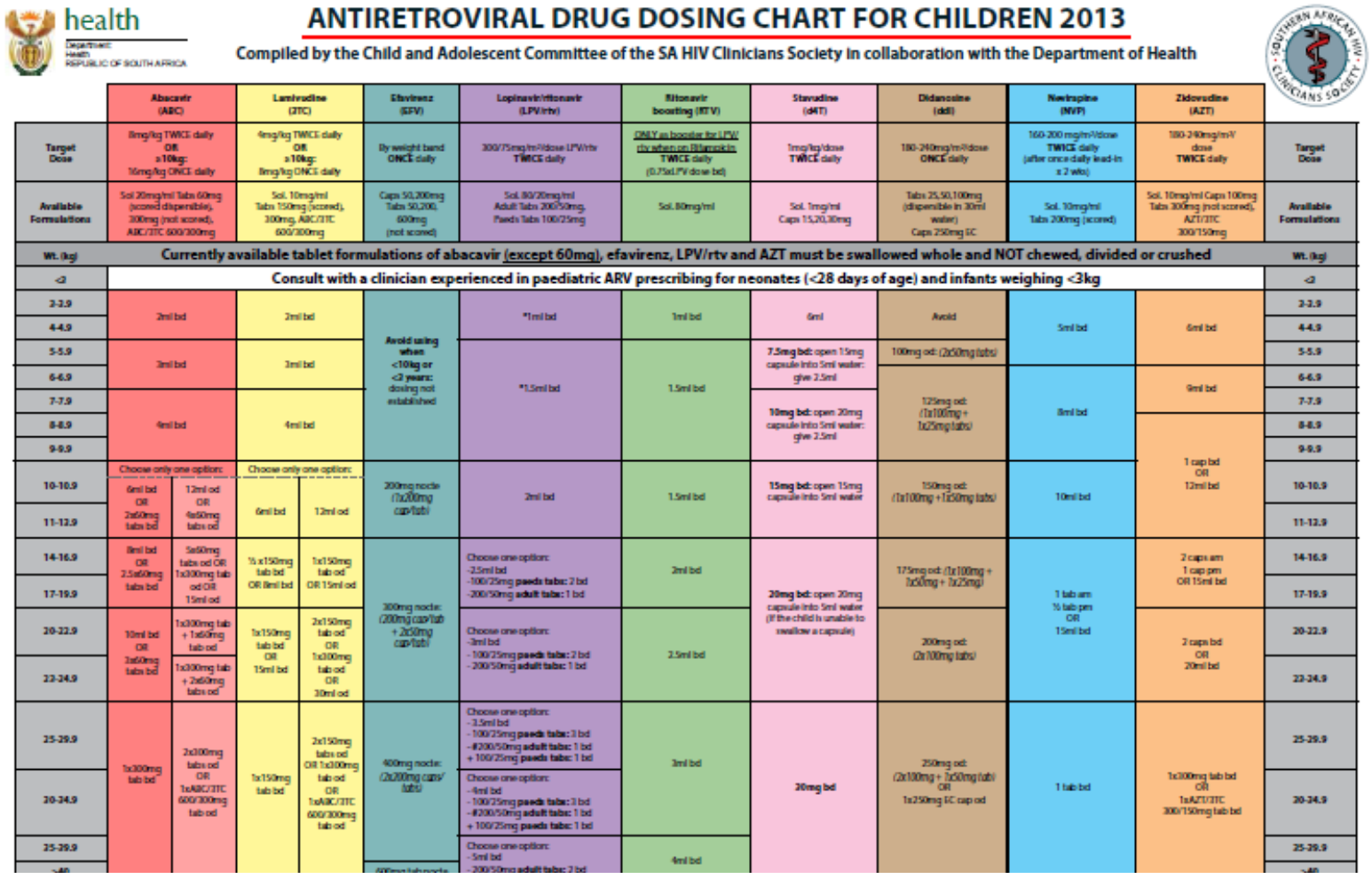


12.4 ANNEXURE 4: INFANTS BORN TO MOTHERS WITH TB

- The following neonates are eligible for IPT:
  - TB disease has been excluded on basis of clinical, radiological (CXR) and bacteriological (gastric aspirates) assessments and
  - Mother is non-infectious and has drug susceptible TB[2]
- If eligible, prescribe INH 10mg/kg daily for 6 months (see dosing table above)[2]



12.5 ANNEXURE 5: PAEDIATRIC ARV DOSING CHART FOR CHILDREN



health
Department: Health
REPUBLIC OF SOUTH AFRICA

ANTIRETROVIRAL DRUG DOSING CHART FOR CHILDREN 2013

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)
<2	Consult with a clinician experienced in paediatric ARV prescribing for neonates (<28 days of age) and infants weighing <3kg											<2
2-3.9	2ml bd		2ml bd		Avoid using when <10kg or <2 years: dosing not established	*1ml bd	1ml bd	6ml	Avoid	5ml bd	6ml bd	2-3.9
4-4.9												4-4.9
5-5.9	3ml bd		3ml bd			*1.5ml bd	1.5ml bd	7.5mg bd: open 1.5mg 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
11-12.9												11-12.9
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 + 2x50mg + 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												>40

12.6 ANNEXURE 6: CREATININE CLEARANCE TABLES

These tables are provided to assist with manual calculation. Please note though that the new NHLS forms incorporate creatinine clearance calculation (see form following these tables) using 3 data points: gender, age and weight.

Creatinine Clearance in ml/min

$$\frac{(140\text{-age}) \times \text{weight in kg} \times 1.04}{\text{pCr in umol/liter}}$$

Table 1: Female, age 15-40 years

Weight in kg	30-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70
	30 35	36 40	41 45	46 50	51 55	56 60	61 65	66 70
PCr in umol/liter								
60	52 to 76	62 to 87	71 to 98	80 to 108	88 to 119	97 to 130	106 to 141	114 to 152
70	45 to 65	53 to 74	61 to 84	68 to 93	76 to 102	83 to 111	91 to 121	98 to 130
80	39 to 57	47 to 65	53 to 73	60 to 81	66 to 89	73 to 98	79 to 106	86 to 114
90	35 to 51	42 to 58	48 to 65	53 to 72	59 to 79	65 to 87	70 to 94	76 to 101
100	31 to 46	37 to 52	43 to 59	48 to 65	53 to 72	58 to 78	63 to 85	69 to 91
110	28 to 41	34 to 47	39 to 53	43 to 59	48 to 65	53 to 71	58 to 77	62 to 83
120	26 to 38	31 to 43	36 to 49	40 to 54	44 to 60	49 to 65	53 to 70	57 to 76
130	24 to 35	29 to 40	33 to 45	37 to 50	41 to 55	45 to 60	49 to 65	53 to 70
140	22 to 33	27 to 37	31 to 42	34 to 46	38 to 51	42 to 56	45 to 60	49 to 65
…								
290	11 to 16	11 to 18	15 to 20	16 to 22	18 to 25	20 to 27	22 to 29	24 to 31
300	10 to 15	16 to 17	14 to 20	16 to 22	18 to 24	19 to 26	21 to 28	23 to 30
350	9 to 13	13 to 15	12 to 17	14 to 19	15 to 20	17 to 22	18 to 24	20 to 26
400	8 to 11	12 to 13	11 to 15	12 to 16	13 to 18	15 to 20	16 to 21	17 to 23
450	7 to 10	10 to 12	10 to 13	11 to 14	12 to 16	13 to 17	14 to 19	15 to 20
500	6 to 9	9 to 10	9 to 12	10 to 13	11 to 14	12 to 16	13 to 17	14 to 18
550	6 to 8	9 to 9	8 to 11	9 to 12	10 to 13	11 to 14	12 to 15	12 to 17
600	5 to 8	8 to 9	7 to 10	8 to 11	9 to 12	10 to 13	11 to 14	11 to 15
650	5 to 7	7 to 8	7 to 9	7 to 10	8 to 11	9 to 12	10 to 13	11 to 14
700	7 to 12	10 to 14	9 to 8	7 to 9	8 to 10	8 to 11	9 to 12	10 to 13

Creatinine Clearance in ml/min

$$\frac{(140\text{-age}) \times \text{weight in kg} \times 1.04}{\text{pCr in umol/liter}}$$

Table 2: Female, age 41-65 years

weight in kg	30-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70
	30 35	36 40	41 45	46 50	51 55	56 60	61 65	66 70
PCr in umol/liter								
40	**59** *to* **90**	**70** *to* **103**	**80** *to* **116**	**90** *to* **129**	**99** *to* **142**	**109** *to* **154**	**119** *to* **167**	**129** *to* **180**
50	**47** *to* **72**	**56** *to* **82**	**64** *to* **93**	**72** *to* **103**	**80** *to* **113**	**87** *to* **124**	**95** *to* **134**	**103** *to* **144**
60	**39** *to* **60**	**47** *to* **69**	**53** *to* **77**	**60** *to* **86**	**66** *to* **94**	**73** *to* **103**	**79** *to* **112**	**86** *to* **120**
70	**33** *to* **51**	**40** *to* **59**	**46** *to* **66**	**51** *to* **74**	**57** *to* **81**	**62** *to* **88**	**68** *to* **96**	**83** *to* **103**
80	**29** *to* **45**	**35** *to* **51**	**40** *to* **58**	**45** *to* **64**	**50** *to* **71**	**55** *to* **77**	**59** *to* **84**	**73** *to* **90**
90	**26** *to* **40**	**31** *to* **46**	**36** *to* **51**	**40** *to* **57**	**44** *to* **63**	**49** *to* **69**	**53** *to* **74**	**65** *to* **80**
100	**23** *to* **36**	**28** *to* **41**	**32** *to* **46**	**36** *to* **51**	**40** *to* **57**	**44** *to* **62**	**48** *to* **67**	**58** *to* **72**
110	**21** *to* **33**	**26** *to* **37**	**29** *to* **42**	**33** *to* **47**	**36** *to* **51**	**40** *to* **56**	**43** *to* **61**	**53** *to* **66**
120	**20** *to* **30**	**23** *to* **34**	**27** *to* **39**	**30** *to* **43**	**33** *to* **47**	**36** *to* **51**	**40** *to* **56**	**49** *to* **60**
…								
220	**11** *to* **16**	**13** *to* **19**	**15** *to* **21**	**16** *to* **23**	**18** *to* **26**	**20** *to* **28**	**22** *to* **30**	**27** *to* **33**
230	**10** *to* **16**	**12** *to* **18**	**14** *to* **20**	**16** *to* **22**	**17** *to* **25**	**19** *to* **27**	**21** *to* **29**	**25** *to* **31**
300	**8** *to* **12**	**9** *to* **14**	**11** *to* **15**	**12** *to* **17**	**13** *to* **19**	**15** *to* **21**	**16** *to* **22**	**19** *to* **24**
350	**7** *to* **10**	**8** *to* **12**	**9** *to* **13**	**10** *to* **15**	**11** *to* **16**	**12** *to* **18**	**14** *to* **19**	**17** *to* **21**
400	**6** *to* **9**	**7** *to* **10**	**8** *to* **12**	**9** *to* **13**	**10** *to* **14**	**11** *to* **15**	**12** *to* **17**	**15** *to* **18**
450	**5** *to* **8**	**6** *to* **9**	**7** *to* **10**	**8** *to* **11**	**9** *to* **13**	**10** *to* **14**	**11** *to* **15**	**13** *to* **16**
500	**5** *to* **7**	**6** *to* **8**	**6** *to* **9**	**7** *to* **10**	**8** *to* **11**	**9** *to* **12**	**10** *to* **13**	**12** *to* **14**
550	**4** *to* **7**	**5** *to* **7**	**6** *to* **8**	**7** *to* **9**	**7** *to* **10**	**8** *to* **11**	**9** *to* **12**	**11** *to* **13**
600	**4** *to* **6**	**5** *to* **7**	**5** *to* **8**	**6** *to* **9**	**7** *to* **9**	**7** *to* **10**	**8** *to* **11**	**10** *to* **12**

Creatinine Clearance in ml/min

$$\frac{(140\text{-age}) \times \text{weight in kg} \times 1.23}{\text{pCr in umol/liter}}$$

Table 3: Male, age 15-40 years

weight in kg	30-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70
	30 35	36 40	41 45	46 50	51 55	56 60	61 65	66 70
PCr in umol/liter								
70	**53** *to* **77**	**63** *to* **88**	**72** *to* **99**	**81** *to* **110**	**90** *to* **121**	**98** *to* **132**	**107** *to* **143**	**116** *to* **154**
80	**46** *to* **67**	**55** *to* **77**	**63** *to* **86**	**71** *to* **96**	**78** *to* **106**	**86** *to* **115**	**94** *to* **125**	**101** *to* **135**
90	**41** *to* **60**	**49** *to* **68**	**56** *to* **77**	**63** *to* **85**	**70** *to* **94**	**77** *to* **103**	**83** *to* **111**	**90** *to* **120**
100	**37** *to* **54**	**44** *to* **62**	**50** *to* **69**	**57** *to* **77**	**63** *to* **85**	**69** *to* **92**	**75** *to* **100**	**81** *to* **108**
110	**34** *to* **49**	**40** *to* **56**	**46** *to* **63**	**51** *to* **70**	**57** *to* **77**	**63** *to* **84**	**68** *to* **91**	**74** *to* **98**
120	**31** *to* **45**	**37** *to* **51**	**42** *to* **58**	**47** *to* **64**	**52** *to* **70**	**57** *to* **77**	**63** *to* **83**	**68** *to* **90**
130	**28** *to* **41**	**34** *to* **47**	**39** *to* **53**	**44** *to* **59**	**48** *to* **65**	**53** *to* **71**	**58** *to* **77**	**62** *to* **83**
140	**26** *to* **38**	**32** *to* **44**	**36** *to* **49**	**40** *to* **55**	**45** *to* **60**	**49** *to* **66**	**54** *to* **71**	**58** *to* **77**
150	**25** *to* **36**	**30** *to* **41**	**34** *to* **46**	**38** *to* **51**	**42** *to* **56**	**46** *to* **62**	**50** *to* **67**	**54** *to* **72**
160	**23** *to* **34**	**28** *to* **38**	**32** *to* **43**	**35** *to* **48**	**39** *to* **53**	**43** *to* **58**	**47** *to* **62**	**51** *to* **67**
170	**22** *to* **32**	**26** *to* **36**	**30** *to* **41**	**33** *to* **45**	**37** *to* **50**	**41** *to* **54**	**44** *to* **59**	**48** *to* **63**
…								
350	**11** *to* **15**	**13** *to* **18**	**14** *to* **20**	**16** *to* **22**	**18** *to* **24**	**20** *to* **26**	**21** *to* **29**	**23** *to* **31**
400	**9** *to* **13**	**11** *to* **15**	**13** *to* **17**	**14** *to* **19**	**16** *to* **21**	**17** *to* **23**	**19** *to* **25**	**20** *to* **27**
450	**8** *to* **12**	**10** *to* **14**	**11** *to* **15**	**13** *to* **17**	**14** *to* **19**	**15** *to* **21**	**17** *to* **22**	**18** *to* **24**
500	**7** *to* **11**	**9** *to* **12**	**10** *to* **14**	**11** *to* **15**	**13** *to* **17**	**14** *to* **18**	**15** *to* **20**	**16** *to* **22**
550	**7** *to* **10**	**8** *to* **11**	**9** *to* **13**	**10** *to* **14**	**11** *to* **15**	**13** *to* **17**	**14** *to* **18**	**15** *to* **20**
600	**6** *to* **9**	**7** *to* **10**	**8** *to* **12**	**9** *to* **13**	**10** *to* **14**	**11** *to* **15**	**13** *to* **17**	**14** *to* **18**
650	**6** *to* **8**	**7** *to* **9**	**8** *to* **11**	**9** *to* **12**	**10** *to* **13**	**11** *to* **14**	**12** *to* **15**	**12** *to* **17**
700	**5** *to* **8**	**6** *to* **9**	**7** *to* **10**	**8** *to* **11**	**9** *to* **12**	**10** *to* **13**	**11** *to* **14**	**12** *to* **15**
750	**5** *to* **7**	**6** *to* **8**	**7** *to* **9**	**8** *to* **10**	**8** *to* **11**	**9** *to* **12**	**10** *to* **13**	**11** *to* **14**
800	**5** *to* **7**	**6** *to* **8**	**6** *to* **9**	**7** *to* **10**	**8** *to* **11**	**9** *to* **12**	**9** *to* **12**	**10** *to* **13**

Creatinine Clearance in ml/min

(140-age) x weight in kg x 1.23
pCr in umol/liter

Table 2: Male, age 41-65 years

weight in kg	30-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70
	30 35	36 40	41 45	46 50	51 55	56 60	61 65	66 70
PCr in umol/liter								
50	**55** *to* **85**	**66** *to* **97**	**76** *to* **110**	**85** *to* **122**	**94** *to* **134**	**103** *to* **146**	**113** *to* **158**	**122** *to* **170**
60	**46** *to* **71**	**55** *to* **81**	**63** *to* **91**	**71** *to* **101**	**78** *to* **112**	**86** *to* **122**	**94** *to* **132**	**101** *to* **142**
70	**40** *to* **61**	**47** *to* **70**	**54** *to* **78**	**61** *to* **87**	**67** *to* **96**	**74** *to* **104**	**80** *to* **113**	**87** *to* **122**
80	**35** *to* **53**	**42** *to* **61**	**47** *to* **68**	**53** *to* **76**	**59** *to* **84**	**65** *to* **91**	**70** *to* **99**	**76** *to* **107**
90	**31** *to* **47**	**37** *to* **54**	**42** *to* **61**	**47** *to* **68**	**52** *to* **74**	**57** *to* **81**	**63** *to* **88**	**68** *to* **95**
100	**28** *to* **43**	**33** *to* **49**	**38** *to* **55**	**42** *to* **61**	**47** *to* **67**	**52** *to* **73**	**56** *to* **79**	**61** *to* **85**
110	**25** *to* **39**	**30** *to* **44**	**34** *to* **50**	**39** *to* **55**	**43** *to* **61**	**47** *to* **66**	**51** *to* **72**	**55** *to* **77**
120	**23** *to* **36**	**28** *to* **41**	**32** *to* **46**	**35** *to* **51**	**39** *to* **56**	**43** *to* **61**	**47** *to* **66**	**51** *to* **71**
130	**21** *to* **33**	**26** **37**	**29** **42**	**33** **47**	**36** **52**	**40** **56**	**43** **61**	**47** **66**
…								
260	**11** *to* **16**	**13** *to* **19**	**15** *to* **21**	**16** *to* **23**	**18** *to* **26**	**20** *to* **28**	**22** *to* **30**	**23** *to* **33**
300	**9** *to* **14**	**11** *to* **16**	**13** *to* **18**	**14** *to* **20**	**16** *to* **22**	**17** *to* **24**	**19** *to* **26**	**20** *to* **28**
350	**8** *to* **12**	**9** *to* **14**	**11** *to* **16**	**12** *to* **17**	**13** *to* **19**	**15** *to* **21**	**16** *to* **23**	**17** *to* **24**
400	**7** *to* **11**	**8** *to* **12**	**9** *to* **14**	**11** *to* **15**	**12** *to* **17**	**13** *to* **18**	**14** *to* **20**	**15** *to* **21**
450	**6** *to* **9**	**7** *to* **11**	**8** *to* **12**	**9** *to* **14**	**10** *to* **15**	**11** *to* **16**	**13** *to* **18**	**14** *to* **19**
500	**6** *to* **9**	**7** *to* **10**	**8** *to* **11**	**8** *to* **12**	**9** *to* **13**	**10** *to* **15**	**11** *to* **16**	**12** *to* **17**
550	**5** *to* **8**	**6** *to* **9**	**7** *to* **10**	**8** *to* **11**	**9** *to* **12**	**9** *to* **13**	**10** *to* **14**	**11** *to* **15**
600	**5** *to* **7**	**6** *to* **8**	**6** *to* **9**	**7** *to* **10**	**8** *to* **11**	**9** *to* **12**	**9** *to* **13**	**10** *to* **14**

12.7 ANNEXURE 7: GRADING OF ADVERSE EVENTS IN ADULTS AND CHILDREN

SOURCE: DIVISION OF AIDS TABLE FOR GRADING THE SEVERITY OF ADULT AND PEDIATRIC ADVERSE EVENTS, VERSION 1.0, DECEMBER 2004; CLARIFICATION AUGUST 2009

Feature	Grade 1	Grade 2	Grade 3	Grade 4
Haematology				
Haemoglobin Infant 1-21 days	12.0-13.0 g/dL	10.0-11.9 g/dL	9.0-9.9g/dL	< 9.0g/dL
Haemoglobin Infant 22-35 days	9.5-10.5g/dL	8.0-9.4 g/dL	7.0-7.9g/dL	< 7.0g/dL
Haemoglobin Infant 36-56 days	8.5-9.4g/dL	7.0-8.4g/dL	6.0-6.9g/dL	< 6.0g/dL
Hb ≥ 57 days (HIV-positive only)	8.5-10.0g/dL	7.5-8.4g/dL	6.5-7.4g/dL	< 6.5g/dL
Absolute neutrophil count Infant 1 day	4.0-5.0x109/l	3.0-3.9x109/l	1.5-2.9x 109/l	< 1.5 x 109/l
Absolute neutrophil count Infant 2 – 7days	1.25-1.5x109/l	1.0-1.24x109/l	0.75-0.99x109/l	< 0.75x109/l
Absolute neutrophil count Children ≥7 days	1.0-1.3 x109/l	0.75-0.9 x109/l	0.5-0.75 x109/l	< 0.5 x109/l
Platelets (cells/ µl)	100,000– 124,999 /mm^3	50,000–99,999 /mm^3	25,000 –49,999 /mm^3	<25,000/mm^3 or bleeding
Gastro-intestinal				
Bilirubin	1.1–1.5 x ULN	1.6–2.5 x ULN	2.6 – 5.0 x ULN	>5 x ULN
AST	1.25–2.5 x ULN	2.6– 5.0 x ULN	5.1– 10.0 x ULN	> 10.0 x ULN
ALT	1.25– 2.5 x ULN	2.6-5.0 x ULN	5.1– 10.0 x ULN	> 10.0 x ULN
γGT	1.1 – 4.9 x ULN	5.0 – 9.9 x ULN	10.0 – 15.0 x ULN	> 15.0 x ULN
Pancreatic Amylase	1.1–1.5 x ULN	1.6 – 2.0 x ULN	2.1 –5.0 x ULN	> 5.0 x ULN
Diarrhoea Adult and paediatric ≥ 1 year	Transient or intermittent episodes of unformed stools OR Increase of ≤ 3 stools over baseline per 24-hour period	Persistent episodes of unformed to watery stools OR Increase of4 – 6 stools over baseline per 24-hourperiod	Bloody diarrhoea OR Increase of ≥7 stools per 24-hour period OR IV fluid replacement indicated	Life-threatening consequences (e.g., hypotensive shock)
Diarrhoea Paediatric < 1year	Liquid stools (more unformed than usual)but	Liquid stools with increased number	Liquid stools with moderate dehydration	Liquid stools resulting in severe dehydration with

Feature	Grade 1	Grade 2	Grade 3	Grade 4
	usual number of stools	of stools OR Mild dehydration		aggressive rehydration indicated OR Hypotensive shock
Constipation	NA	Persistent constipation requiring regular use of dietary modifications, laxatives, or enemas	Obstipation with manual evacuation indicated	Life-threatening consequences (e.g., obstruction)
Nausea	Transient (<24 hours) or intermittent nausea with no or minimal interference with oral intake	Persistent nausea resulting in decreased oral intake for 24 – 48 hours	Persistent nausea resulting in minimal oral intake for >48 hours OR Aggressive rehydration indicated (e.g., IV fluids)	Life-threatening consequences (e.g., hypotensive shock)
Vomiting	Transient or intermittent vomiting with no or minimal interference with oral intake	Frequent episodes of vomiting with no or mild dehydration	Persistent vomiting resulting in orthostatic hypotension OR Aggressive rehydration indicated (e.g., IV fluids)	Life-threatening consequences (e.g., hypotensive shock)
Allergic / Dermatological				
Acute systemic allergic reaction	Localised urticarial (wheals) with no medical intervention indicated	Localised urticaria with medical intervention indicated OR Mild angioedema with no medical intervention indicated	Generalised urticaria OR Angioedema with medical intervention indicated OR Symptomatic mild bronchospasm	Acute anaphylaxis OR Life-threatening bronchospasm OR Laryngeal oedema
Cutaneous reaction-skin rash*	Localised macular rash	Diffuse maculopapular rash OR Morbilliform rash	Diffuse macular, maculopapular, or morbilliform rash with vesicles or limited number of	Extensive/ generalized bullous lesions OR Stevens-Johnson

Feature	Grade 1	Grade 2	Grade 3	Grade 4
		OR Target lesions	bullae OR Superficial ulcerations of mucous membrane limited to one site	syndrome OR laceration of mucous membrane involving two or more distinct mucosal sites OR Toxic Epidermal Necrolysis (TEN)
Nervous system				
Developmental delay– Paediatric <1 Years	Mild developmental delay, either motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting	Moderate developmental delay, motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting	Severe developmental delay, either motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting	Developmental regression, either motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting
Neuromuscular weakness(including myopathy and neuropathy)	Asymptomatic with decreased strength on exam OR Minimal muscle weakness causing no or minimal interference with usual social and functional activities	Muscle weakness causing greater than minimal interference with usual social and functional activities	Muscle weakness causing inability to perform usual social and functional activities	Disabling muscle weakness causing inability to perform basic self-care functions OR Respiratory muscle weakness impairing ventilation
Neurosensory alteration (including paraesthesia and painful neuropathy)	Asymptomatic with sensory alteration on exam or minimal paraesthesia causing no or minimal interference with usual social and functional activities	Sensory alteration or paraesthesia causing greater than minimal interference with usual social and functional activities	Sensory alteration causing inability to perform usual social and functional activities	Disabling sensory alteration or paraesthesia causing inability to perform basic self-care functions
Other				
Clinical symptoms not otherwise specified above	No therapy, monitor condition	May require minimal intervention and	Requires medical care or possible	Requires active medical intervention,

Feature	Grade 1	Grade 2	Grade 3	Grade 4
		monitoring	hospitalisation	hospitalisation or hospice care

12.8 ANNEXURE 8: GUIDELINES FOR ADVERSE DRUG REACTION REPORTING

National Pharmacovigilance Programme

The Medicines Control Council (MCC) has a responsibility to ensure the safety, efficacy and quality of all medicines used by the South African public. The National Pharmacovigilance Programme is coordinated by the MCC and has two dedicated units responsible for the monitoring the safety of medicines. The National Adverse Drug Event Monitoring Centre (NADEMC) in Cape Town monitors the safety of all registered medicines in South Africa. In addition, a focused surveillance unit at MEDUNSA is responsible for monitoring the safety of ARVs and complementary medicines. The unit at MEDUNSA is also responsible for monitoring the safety of unregistered medicines used during clinical trials.

What is Pharmacovigilance?

Pharmacovigilance is defined as the science and activities concerned with the detection, assessment, understanding and prevention of adverse reactions to medicines (i.e. adverse drug reactions). The ultimate goal of this activity is to improve the safe and rational use of medicines, thereby improving patient care and public health.

What is an Adverse Drug Reaction (ADR)?

The Medicines Control Council (MCC) defines an Adverse Drug Reaction (ADR) 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 overdose, misuse or abuse of a medicine.

Who should report Adverse Drug Reactions?

All healthcare workers, including doctors, dentists, pharmacists, nurses and other health professionals are encouraged to report all suspected adverse reactions to medicines (including vaccines, X-ray contrast media, traditional and herbal remedies), especially when the reaction is not in the package insert, potentially serious or clinically significant.

What happens to a report?

All ADR reports are entered into a national ADR database. Each report is evaluated to assess the causal relationship between the event and the medicine. A well-completed adverse drug reaction/product quality form submitted could result in any of the following:

- Additional investigations into the use of the medicine in South Africa
- Educational initiatives to improve the safe use of the medicine
- Appropriate package insert changes to include the potential for the reaction
- Changes in the scheduling or manufacture of the medicine to make it safer

The purpose of ADR reporting is to reduce the risks associated with the use of medicines and to ultimately improve patient care.

Will reporting have any negative consequences on the health worker or the patient?

An adverse drug reaction report does not constitute an admission of liability or that the health professional contributed to the event in any way. The outcome of a report, together with any important or relevant information relating to the reaction, will be sent back to the reporter as appropriate. The details of a report are stored in a confidential database. The names of the

reporter or any other health professionals named on a report and the patient will be removed before any details about a specific adverse drug reaction are used or communicated to others. The information is only meant to improve the understanding of the medicines used in the country.

Assessing whether an event is possibly an ADR

The following factors should be considered when an adverse drug reaction is suspected:

1. What exactly is the nature of the reaction? *(Describe the reaction as clearly as possible and where possible provide an accurate diagnosis)*
2. Did the reaction occur within a reasonable time to suggest relationship to starting treatment with the suspected medicine? *(Some reactions occur immediately after administration of a medicine while others take time to develop)*
3. Is the reaction known to occur with the particular medicine as stated in the package insert or other reference? *(If the reaction is not documented in the package insert, it does not mean that the reaction cannot occur with that particular medicine)*
4. Did the patient recover when the suspected medicine was stopped? *(Some reactions can cause permanent damage, but most reactions are reversible if the medication is stopped)*
5. Did the patient take the medicine again after the reaction abated (i.e. rechallenge). If so, did the same reaction occur again? *(In most situations it is not possible or ethical to rechallenge the patient with the same medicine. If such information is available or if such a rechallenge is necessary, recurrence of the event it is a strong indicator that the medicine is may be responsible*
6. Can this reaction be explained by other causes (e.g. underlying disease/s; other medicine/s; toxins or foods)? *(It is essential that the patient be thoroughly investigated to decide what the actual cause of any new medical problem is. A medicine-related cause should be considered, when other causes do not explain the patient's condition)*

What types of reactions should be reported?

The following adverse drug reactions should be reported:

- All ADRs to newly marketed drugs or new drugs added to the EDL
- All serious reactions and interactions
- ADRs 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 the medicine caused the event

What product quality problems should be reported?

The following product quality problems should be reported:

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

How can ADRs be prevented from occurring?

Some ADRs are unavoidable and cannot be prevented. However, most ADRs can be prevented by following the basic principles of rational use of medicines.

How are adverse drug reactions reported?

An adverse drug reaction/product quality report form is enclosed in this book and should be completed in as much detail as possible before returning it by fax or post to any of the addresses provided below. Additional forms can be obtained by contacting the MCC at these addresses. Report forms may also be accessed via the following website: *http://www.mccza.com*

1. **The Registrar of Medicines**

   Medicines Control Council, Department of Health, Private Bag X828
   Pretoria, 0001
   Tel: (012) 395 9288

2. **The National Adverse Drug Event Monitoring Centre (NADEMC)**

   C/o Division of Pharmacology, University of Cape Town
   Observatory, 7925
   Tel: (021) 447 1618

ADVERSE DRUG REACTION AND PRODUCT QUALITY PROBLEM REPORT FORM

(*Identities of reporter and patient will remain strictly confidential)*

health

Department:
Health
REPUBLIC OF SOUTH AFRICA

NATIONAL ADVERSE DRUG EVENT MONITORING CENTRE

NADEMC

The Registrar of Medicines
Private Bag X 828
Pretoria, 0001

Fax: (021) 448-6181
Tel: (021) 447-1618

In collaboration with the WHO International Drug Monitoring Programme

PATIENT INFORMATION

Name (or initials): ..... **Patient Reference Number:** ……

Sex: | **M** | **F** | **Age:** ..... **DOB:** ..... / ...../ ..... **Weight (kg)** ..... **Height (cm)** .....

ADVERSE REACTION / PRODUCT QUALITY PROBLEM (tick appropriate box)

Adverse reaction ☐ **and/or Product Quality problem** ☐ **Date of onset of reaction:** ...../...../.....

Time of onset of reaction: ..... hour..... min

Description of reaction or problem (Include relevant tests/lab data, including dates):

1. MEDICINES / VACCINES / DEVICES (include all concomitant medicines)

Trade Name & Batch No. (Asterisk Suspected Product)	Daily Dosage	Route	Date Started	Date Stopped	Reasons for use

ADVERSE REACTION OUTCOME (Check all that apply)

☐ Death
☐ Disability
☐ Congenital anomaly
☐ Required intervention to prevent permanent

☐ Life-threatening
☐ Hospitalisation
☐ Other.....
.....

Reaction abated after stopping medicine: **Y** ☐ **N** ☐ **N/A** ☐

Event reappeared **Y** ☐ **Rechallenge not done** ☐

Recovered: **Y** ☐ **N** ☐

Sequelae: **Y** ☐ **N** ☐

Describe Sequelae:.....
.....
.....

impairment/damage	.....	**on rechallenge:**	.....
	.....	**N**	.....
	.....		.....
	.....		.....
	.....		.....

COMMENTS: (e.g. Relevant history, Allergies, Previous exposure, Baseline test results/lab data)

2. PRODUCT QUALITY PROBLEM:

Trade Name	Batch No	Registration No	Dosage form & strength	Expiry Date	Size/Type of container

Product available for evaluation? **Y** **N**

REPORTING HEALTHCARE PROFESSIONAL:

NAME: ..... QUALIFICATIONS:.....

ADDRESS: .....

..... …….. ……..

Signature Date

Postal Code: …… TEL: (.....).....

This report does not constitute an admission that medical personnel or the product caused or contributed to the event

ADVICE ABOUT VOLUNTARY REPORTING

Report adverse experiences with:

- Medications (drugs, vaccines and biologicals)
- Medical devices (including in-vitro diagnostics)
- Complementary / alternative medicines (including traditional, herbal remedies, etc.)

Please report especially:

- Adverse drug reactions to newly marketed products
- Serious reactions and interactions with all products
- Adverse drug reactions that are not clearly reflected in the package insert.

Report product quality problems such as:

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

Report even if:

- You're not certain the product caused the event
- You don't have all the details

Important numbers:

Registered Medicines and Traditional and Herbal remedies

- Fax: 021 448 6181
- Tel: 021 447 1618

Investigational Products and Product Quality Problems

- Fax: 012 395 9201
- Tel: 012 395 9341

Adverse Events Following Immunisation

- Fax: 012 395 8905
- Tel: 012 395 8914/5

Confidentiality: Identities of the reporter and patient will remain strictly confidential.

Your support of the Medicine Control Council's adverse drug reaction monitoring programme is much appreciated. Information supplied by you will contribute to the improvement of medicine safety and therapy in South Africa.