Applications, comments and inquiries should be addressed to the Secretary for Health, P.O. Box 30377, Lilongwe 3, Malawi. We will be glad to provide the latest information on any changes made to the text, plans for new editions, and reprints and translations already available.

An electronic copy of this guideline is available on the website (www.hiv.health.gov.mw) of the Dept. for HIV and AIDS of the Ministry of Health.

NOTE: The mention of certain manufacturers' products does not imply they are endorsed or recommended by the Ministry of Health in preference to others of a similar nature that are not mentioned.

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Foreword to the 4th Edition

This 4th *Edition* of the *Malawi Guidelines for Clinical Management of HIV in Children and Adults* will be implemented from July 2018. It replaces all previous editions of the Malawi Antiretroviral therapy (ART) and Prevention of Mother to Child Transmission (PMTCT) guidelines.

This document is written for medical doctors, clinical officers, medical assistants, nurses, midwives, laboratorians, health surveillance assistants (HSAs) and medical records clerks who are working in public and private sector health facilities in Malawi. It is designed to be a practical guide for implementation of integrated HIV Services.

The guidelines have been compiled by the joint Technical Working Groups for PMTCT, ART, HIV testing and Paediatric HIV under the leadership of the Dept. for HIV and AIDS of the Ministry of Health. The guidelines are based on ***Malawi's Revised Policy for PMTCT and ART*** which was endorsed by the Ministry of Health in June 2010 and which was prompted by the release of the 2010 Revision of the World Health Organisation (WHO) PMTCT and ART Guidelines. This 4th Edition is an adaptation of the latest WHO Recommendations[1].

The protocols and policies presented in this document are adapted for health services in Malawi and follow a ***public health approach,*** aiming to provide the best possible services for the largest possible number of persons in need of these services.

Universal ART eligibility for all PLHIV was introduced in the **2016** edition of these guidelines, following clear scientific evidence that patients should **start ART as soon as possible** after getting infected with HIV. **Patient benefits**: reduced risk of serious HIV-related illnesses that can occur even in the early stages of HIV infection when the CD4 count is still above 500. Early treatment benefits outweigh the risk of side effects because the regimens are easy to take and usually well tolerated.

[1] HIV Treatment: Transition to new antiretrovirals in HIV Programs (WHO Policy Brief July 2017)
Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy (WHO July 2017)
What's new in treatment monitoring: viral load and CD4 testing (WHO July 2017)
Key considerations for differentiated antiretroviral therapy delivery for specific populations: children, adolescents, pregnant and breastfeeding women and key populations. (WHO 2017).
What's new in infant diagnosis (WHO 2015)
Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach – 2nd ed. (WHO 2016)

Population benefits: successful ART greatly reduces the risk of onward transmission to sexual partners and from mother to child.

The National Strategic Plan for HIV (2015-2020) includes the **90-90-90 treatment targets** put forward by UNAIDS, aiming to achieve viral suppression for 73% of the total HIV infected population by 2020. This will greatly reduce the number of new HIV infections and is expected to achieve epidemic control in the longer term. The 90-90-90 strategy requires further streamlining of HIV program policies. By mid-2018, Malawi is **well on track** to achieving these targets.

This 4th Edition of the Malawi Clinical HIV Guidelines introduces **dolutegravir** (**DTG**) as a further optimization of ART regimens. A blanket transition to DTG-based regimens for eligible patient groups is planned for January 2019.

This document defines the framework for Malawi's National HIV Programs. Considering public health benefits and risks, as well as funding and resource implications, **deviations from these guidelines are not supported by the Ministry of Health**.

Foreword to the 1st Edition

This 1st Edition of the Malawi Guidelines for Clinical Management if HIV in Children and Adults will be implemented from July 2011. It replaces all previous editions of the Malawi Antiretroviral Therapy (ART) and Prevention of Mother to Child Transmission (PMTCT) guidelines.

These guidelines are written for medical doctors, clinical officers, medical assistants, nurses, midwives, health surveillance assistants (HSAs) and medical records clerks who are working in public and private sector health facilities in Malawi. The document is designed to be a practical guide for implementation of integrated HIV services.

These guidelines have been compiled by the Joint Technical Working Groups for PMTCT, ART, HTC and Paediatric HIV under the leadership of the Department for HIV and AIDS of the Ministry of Health. The guidelines are based on Malawi's revised policy for PMTCT and ART which was endorsed by the Ministry of Health in June 2010 and which was prompted by the release of the 2010 Revision of the 2010 WHO PMTCT and ART guidelines.

The protocols and policies presented in this document are adapted for health services in Malawi and follow a public health approach, aiming to provide the best possible services for the largest possible number of persons in need of these services.

This document defines the framework for Malawi's National HIV Programs. Considering public health benefits and risks, as well as funding and resource implications, deviations from these guidelines are not supported by the Ministry of Health.

The 2nd Edition of these guidelines is scheduled for release in 2013. Any updates or amendments to protocols and policies that are to be implemented between July 2010 and the release of the 2nd Edition of the guidelines will be communicated through an official MOH circular.

Acronyms and Abbreviations

3TC	Lamivudine
ABC	Abacavir
ANC	Antenatal care
ARM	Artificial rupture of membranes
ART	Antiretroviral therapy
ARVs	Antiretroviral drugs
ATV/r	Atazanavir / ritonavir
AZT	Zidovudine
B6	Pyridoxine
BCG	Bacille Calmette-Guérin
Benzyl pen	Benzyl penicillin
BF	Breastfeeding
BMI	Body mass index
CO	Clinical Officer
CPT	Cotrimoxazole preventive therapy
CrAg	Cryptococcal antigen
CSF	Cerebrospinal fluid
CTX	Cotrimoxazole
CXR	Chest X-ray
DBS	Dried blood spot
dl	decilitre
DL	Detection limit (for viral load)
DNA-PCR	Deoxyribonucleic acid polymerase chain reaction
DTG	Dolutegravir
E	Ethambutol
EFV	Efavirenz
EMB	Ethambutol
EPI	Extended Programme on Immunization
EPTB	Extra-pulmonary tuberculosis
FDC	Fixed dose combination
FP	Family planning
GIT	Gastrointestinal tract
H	Isoniazid
Hb	Haemoglobin
HCC	HIV Care Clinic
HIV	Human immunodeficiency virus
HTS	HIV testing services
IEC	Information, Education and Communication
IM	Intramuscular
INH	Isoniazid

Acronyms and Abbreviations

INSTI	Integrase strand transfer inhibitor
IPT	Isoniazid preventive therapy
IRIS	Immune reconstitution inflammatory syndrome
ITN	Insecticide treated net
IV	Intravenous
KS	Kaposi sarcoma
LAM (urine-)	Mycobacterial lipoarabinomannan (LAM) antigen in urine
LFT	Liver function test
LPV/r	Lopinavir/ ritonavir
MA	Medical Assistant
MCH	Maternal and child health
MDR-TB	Multi-drug resistant tuberculosis
MUAC	Mid-upper arm circumference
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
NS	Non-standard (ART regimen)
NVP	Nevirapine
OPD	Out-patient Dept.
ORS	Oral rehydration solution
PCP	Pneumocystis carinii (jiroveci) pneumonia
PCR	Polymerase chain reaction
PEP	Post-exposure prophylaxis for HIV using antiretroviral medicines
PI	Protease inhibitor
PIFP	Provider initiated family planning
PMTCT	Prevention of mother to child transmission
PO	Per os
PrEP	Pre-exposure prophylaxis for HIV using antiretroviral medicines
PSHD	Presumed severe HIV disease
PTB	Pulmonary tuberculosis
PZA	Pyrazinamide
R	Rifampicin
S	Streptomycin
SP	Sulphadoxine / pyrimethamine
STI	Sexually transmitted infections
TDF	Tenofovir disoproxil fumarate
TF	Therapeutic feeding
VIA	Visual inspection (of the cervix) with acetic acid
VL	Viral load
ZDV	Zidovudine

1 How to use these guidelines?

These guidelines standardise clinical management of HIV positive patients and of HIV exposed children using an integrated approach. They also incorporate relevant protocols from other national guidelines (TB, IPT, FP, STI and Reproductive Health).

Most clinical interventions for HIV patients are provided in different service delivery settings. The **standardised simplified protocols** for each intervention presented in this document will facilitate the job of the health workers and improve the standard of care for patients.

Key Facts for Patients and Providers

- The most important information and key instructions are presented in a box at the beginning of each section.
- It is appropriate and helpful to share this information with patients during Information, Education, and Communication (IEC) sessions, and in individual counselling.

Short bullet points and 'plain language' are used throughout this document to make the information as clear and concise as possible.

The standard package of clinical HIV interventions

Chapter 4 on page 11 shows **which** of the **clinical HIV interventions** should be provided in each of the regular service delivery points of the health system. It also defines the standard package of services and explains which interventions are appropriate for which patient groups and **when** to deliver them.

Protocols for how to deliver clinical HIV interventions

Chapters 5 – **21** (page **13** – **94)** explain in detail **how** to deliver each of the HIV interventions. The protocols and directions are the same for *all* service delivery settings. These chapters also contain several checklists, tables and flow charts which can be laminated and used as job aids in the consultation room.

2 Summary of new policies

Key Facts: New Policies

- All HIV infected people should **start ART as soon as possible** for their own health and to prevent passing the virus on to others.
- Serious HIV-related diseases can occur even in patients with high CD4 count (>500), without any previous symptoms. Immediate ART greatly reduces this risk.
- Current ART regimens are easy to take and rarely cause serious side-effects.
- **ART** for all HIV infected people is the **most effective prevention method** available: Successful ART leads to very low levels of virus in the blood and in body fluids (viral suppression). Viral suppression greatly reduces the risk of sexual or mother-to-child transmission.
- **Dolutegravir** (DTG)-based ART regimens will be introduced for eligible patient groups from the beginning of 2019. DTG is promising to be more potent, more durable and cause even fewer side-effects and interactions with other medicines. However, standard ART regimens from the 2016 guidelines remain the best choice for patient groups such as girls and women who may get pregnant while on ART. These regimens and will be retained as standard 1st line regimens for many patients.

Table 1: Key new and updated policies

		Page
HIV-related diseases		
New	Routine screening for disseminated TB and cryptococcal infection in severely ill PLHIV using urine LAM and CrAg rapid tests.	**22**
Old	Fluconazole monotherapy for primary management of cryptococcal meningitis	
New	Short-course Amphotericin B + Flucytosine for induction phase treatment of cryptococcal meningitis.	**23**
Old	Vincristine monotherapy as primary chemotherapy for Kaposi sarcoma (KS)	
New	Paclitaxel as primary chemotherapy for KS	**26**
Standard monitoring of HIV patients		
Old	CD4 counts only for targeted investigation	
New	CD4 counts as routine baseline (if available) and for targeted investigation	**37**
Choosing ART regimen, formulation and dosage		
Old	Regimen 5A (tenofovir/lamivudine/efavirenz) as standard 1st line for all patients from **35**kg+	
New	Regimen 13A (tenofovir/lamivudine/dolutegravir) as standard 1st line for males from 30kg+ and women aged 45 years+ Regimen 5A as standard 1st line for girls and women who may get pregnant while on ART from **30**kg+ Once they have reached 30kg, routinely change all boys from 2A to 13A and all girls from 2A to 5A.	**48** **50** **52**
Old	Adult formulation regimens with tenofovir (300mg) and efavirenz (600mg) can be used from 35kg+	
New	Adult formulation TDF and EFV can be used from 30kg+	**52**
Old	Standard backbone of 3rd line ART is darunavir, ritonavir, raltegravir and etravirine	
New	Standard backbone of 3rd line ART is darunavir, ritonavir and dolutegravir	**52**
Old	11 Standard ART regimens: five 1st line, five 2nd line and one 3rd line regimen	
New	14 standard ART regimens: eight 1st line, five 2nd line and one 3rd line	**52**
Combining ART and TB treatment		
New	Explicit ART regimen sequencing recommendations while on rifampicin-based TB treatment	**68**
Viral load (VL) testing		
Old	Confirmed good adherence in the last 3 months is a condition for collecting a VL sample	
New	Routine and targeted VL samples are collected regardless of good adherence in the last 3 months. Decision to switch to 2nd line ART depends on current regimen. Patients on DTG- or PI-based regimens need genotyping to confirm resistance.	**78**

Differentiated ART services		
New	Three differentiated ART delivery models are offered for eligible patient groups.	**87**
Transition to new ART regimens (2018/2019)		
New	Eligible patients already on ART transition to DTG-based regimens once stocks of the new ARVs have arrived at the site (scheduled for January 2019).	**93**
Post exposure prophylaxis (PEP)		
Old	Four weeks of TDF/3TC is standard PEP regimen for patients from 35kg+	
New	Four weeks of TDF/3TC/DTG is standard PEP regimen for patients from 30kg+	**94**
Pharmacovigilance		
New	New standard tools for reporting of suspected adverse drug reactions.	**98**

3 Implementation plan

- The revised policies come into effect in **July 2018**.
- The policy changes will be communicated by circular to all District Health Offices and facilities.
- PMTCT/ART refresher trainings based on this 4th Edition of the Clinical HIV Guidelines will commence in the first half of 2018.
- Facilities start implementing the new policies when at least 2 health workers have passed the 2018 refresher trainings.
- The next (**5th**) Edition of these guidelines is scheduled for release in **2020/21**. Any potential policy or protocol updates to be implemented before release of the next edition of the guidelines will be communicated through an official MOH circular.

4 Integrating clinical HIV services

HIV services are an integral part of the EHP. This section shows the **standard schedule** for the **minimum package of** clinical HIV interventions to be delivered within the established service points. **Table 2** on page **12** outlines the HIV interventions to be offered at various service delivery points. Refer to the page number for details on how to deliver the specific intervention.

HIV Care Clinic (HCC)

- ***HCC*** is an integration in the same clinic setting for:
    - **HIV exposed children**
    - **ART**
- HCC services should be established in ART and MNCH clinics.
- ***HCC*** is designed to facilitate clinical monitoring, preventive services and ART for family members affected by HIV.
- Make family appointments to encourage family members to attend together for HIV services.
- Family members can be seen in the consultation room at the same time or seen individually if there are sensitive issues to discuss.

Table 2: Integrated provision and scheduling of clinical HIV services

Interventions that are provided only under special circumstances are marked with brackets (●)

HIV Service	*Page*	Schedule	OPD	In-Patients	Fam Plan Clin	ANC	Maternity	Postnatal Clin.	U5 Clinic	Exp Child FUP	ART Clinic	TB Clinic
Diagnosing HIV infection and exposure	*15*	Ascertain status at each visit	●	●	●	●	●	●	●	●	(●)	●
HIV-related diseases	*22*	When diagnosed	●	●		(●)	(●)			●	●	●
Standard monitoring of HIV patients	*31*	At every clinical review visit								●	●	●
Provider initiated family planning (PIFP)	*40*	At every scheduled visit									●	
Cotrimoxazole preventive therapy (CPT)	*41*	At every scheduled visit				●	●			●	●	●
Isoniazid preventive therapy (IPT)	*43*	Dispense for 1, 2 and then 3 monthly thereafter									(●)	
Insecticide treated bed nets (ITN)	*44*	Dispense 1 ITN every 24 months				●			●	●	●	
Infant and child feeding counselling	*90*	At every visit	●			●	●		●	●	●	
Starting ART	*60*	As soon as possible	(●)			●	●	●			●	●
Continuing ART	*71*	Monthly for the 1st 6 months; 3 monthly thereafter	(●)			●		●			●	●
Management of labour and delivery	*88*	On admission					●					
New born care and postnatal	*89*	After delivery					●	●				
Initiating integrated mother/infant follow-up	*89*	At first opportunity when mother known HIV+					●	●	●		●	
Infant NVP prophylaxis	*91*	At first opportunity when mother known HIV+				●	●	●	●	(●)		
Post exposure prophylaxis (PEP)	*94*	As soon as possible after risk exposure	●				●					

5 PMTCT Strategy

Key Facts: PMTCT Strategy

- Multiple strategies are available to prevent the transmission of HIV from mother to child and to reduce the HIV burden among mothers and their children.
- These strategies are grouped into the ***4 Prongs of the national PMTCT*** program.
- Implemented together, these strategies have resulted in a drastic reduction of HIV infections among children. Further scale-up is expected to virtually eliminate new paediatric HIV infections and AIDS deaths among children.
- Key interventions from all 4 PMTCT prongs are covered in these guidelines, but some medical and non-biomedical interventions are beyond the scope of this document and are covered in separate guidelines.

Prong 1: Primary prevention of HIV infection in parents

- Behaviour change communication to reduce risky sexual contacts
    - Separate strategy
- Provision of condoms
    - **Section 10.1** Provider initiated family planning (PIFP)
    - Separate condom strategy
- Voluntary medical male circumcision for HIV negative men to reduce the risk of HIV acquisition and onward transmission
    - Separate MOH guidelines
- Scale-up of HIV testing in high-yield settings for early diagnosis and ART referral
    - **Section 6.1**: Routine ascertainment of HIV infection status for children and adults
- ART provision for all HIV infected adults and children, (regardless of CD4 count and/or clinical stage) to reduce morbidity and mortality and to prevent onward transmission
    - **Section 12.1**: When to start ART
    - **Section 13.7**: Achieving optimal adherence
- Viral load monitoring and timely switch to 2nd or 3rd line for patients on ART to ensure viral suppression and to reduce the risk of onward transmission
    - **Section 13.10**: Monitoring for treatment failure / HIV drug resistance
- Post-exposure prophylaxis
    - **Section 17**: Post exposure prophylaxis (PEP)

Prong 2: Prevention of unintended pregnancies among HIV positive women

- Provider initiated family planning in ART clinics
    - **Section 10.1** Provider initiated family planning (PIFP)
    - Separate MOH guidelines: National Sexual and Reproductive Health and Rights Policy

Prong 3: Preventing transmission of HIV from infected women to their children

- Provider initiated testing at MNCH settings for early HIV diagnosis and ART initiation
    - **Section 6.1**: Routine ascertainment of HIV infection status for children and adults
    - **Section 17.1.1**: HIV status ascertainment at maternity
- Initiation of lifelong ART for all HIV infected pregnant and breastfeeding women (regardless of CD4 count and/or clinical stage) to reduce the risk of transmission to the child.
    - **Section 13.1**: When to start ART
- Safe obstetric practices
    - **Section 17.1.3**: Reduce obstetric risk of HIV transmission
- Provision of infant nevirapine prophylaxis
    - **Section 18.3**: Infant NVP prophylaxis
- Infant feeding advice to reduce the risk of transmission through breastmilk
    - **Section 18.2**: Infant and child feeding counselling

Prong 4: Care, treatment and support for HIV-infected women and their children and families

- **Section 4**: Integrating clinical HIV services
- **Section 6.2**: Routine ascertainment of HIV exposure status for children under 24 months
- **Section 18.1**: Initiating integrated mother/infant follow-up
- **Section 8**: HIV-related diseases
- **Section 10**: Preventive services for HIV patients
- **Section 10.2**: Cotrimoxazole preventive therapy (CPT)
- **Section 10.3**: Isoniazid preventive therapy (IPT)
- **Section 10.4**: Insecticide treated bed nets (ITN)
- **Section 13.5**: Detecting and treating high blood pressure
- **Section 15.8**: Special treatment support for children and adolescents

6 Diagnosing HIV infection and exposure

Key Facts: HIV Testing Strategy

- **Main** HIV testing program goals:
    - **Identify as many** HIV **infected** people **as possible.**
    - Identify them **as early as possible** after getting infected.
    - **Ensure they start ART** as **soon** as possible.
- Additional goal is to link HIV negatives to appropriate prevention services (VMMC, etc.) and to encourage retesting based on the client risk assessment.
- **Provider Initiated Testing:** Ascertain HIV status for all patients attending health services (ANC, maternity, TB, STI, FP, U1 / U5, adult and paediatric wards).
- Remind patients during pre-test education (group or individual) that they can decline HIV testing without any 'fear of punishment' by the health worker.
- Encourage patients to attend testing with their sexual partner. Ensure that all children, regardless of age (including adolescents) of HIV infected parents are tested. Ensure all siblings of HIV-infected children have been tested.
- Enrol all children born to and/or breastfeeding from HIV infected mothers (*'HIV exposed children'*) in the HIV Care Clinic and follow to at least age 24 months or longer if breastfeeding continues.
- From age 12 months, over 95% of children with a positive rapid test are confirmed HIV infected. Therefore, rapid testing should be used to diagnose HIV infection and start ART from age 12 months.
- Examine all children under 12 months of age with confirmed HIV antibodies for clinical conditions that constitute *Presumed Severe HIV Disease* (PSHD, see **section 6.3** on page **19**). All of these need to start ART without delay.
- All patients need a confirmatory HIV rapid test to rule out any possibility of mix-up of test results or fraudulent access to ART (also see **section 13.3** on **page 61**):
    - Before starting ART
    - All children under 24 months who start ART need a confirmatory DNA-PCR using a new DBS sample. This should be collected on the day of starting ART (also see **section 13.3.2** on **page 62**).
- See the **Malawi HIV Testing Services Guidelines** for details on testing modes, quality assurance, etc.

6.1 Routine ascertainment of HIV infection status for children and adults

- Ask every client at every visit about the most recent HIV test and review their health passport for previous HIV test results.
- Offer HIV testing to all patients attending health facilities for any reason, if:
    - never tested
    - tested negative more than 3 months ago (follow risk assessment guidelines)
    - claims to have been tested any time in the past, but without documentation (being on ART counts as documented evidence)
- Routinely document HIV test results on page 6 of the patient's health passport unless the patient declines. For in-patients, also document test result in in-patient notes.

6.2 Routine ascertainment of HIV exposure status for children under 24 months

- Routinely ascertain the mother's HIV status for all children under 24 months of age seen at the U1 / U5 clinic, regardless of whether the child is healthy or sick:
    - Review mother's health passport (page 6) for the latest HIV test result
- Initiate a new HIV rapid test:
    - For the mother:
        - If she is not known to be positive and has not been tested at delivery or thereafter.
    - For the child:
        - If the mother is not available / has died
        - If the child is sick, even if the mother was tested negative during pregnancy or delivery. Mothers may have been recently infected themselves and the risk of onward transmission to the child is very high under these circumstances.
- **Figure 1** on **page 17** shows the conditions for testing of mother and/or child and the actions to be taken.

Figure 1: Ascertainment of HIV exposure / infection in children under 24 months

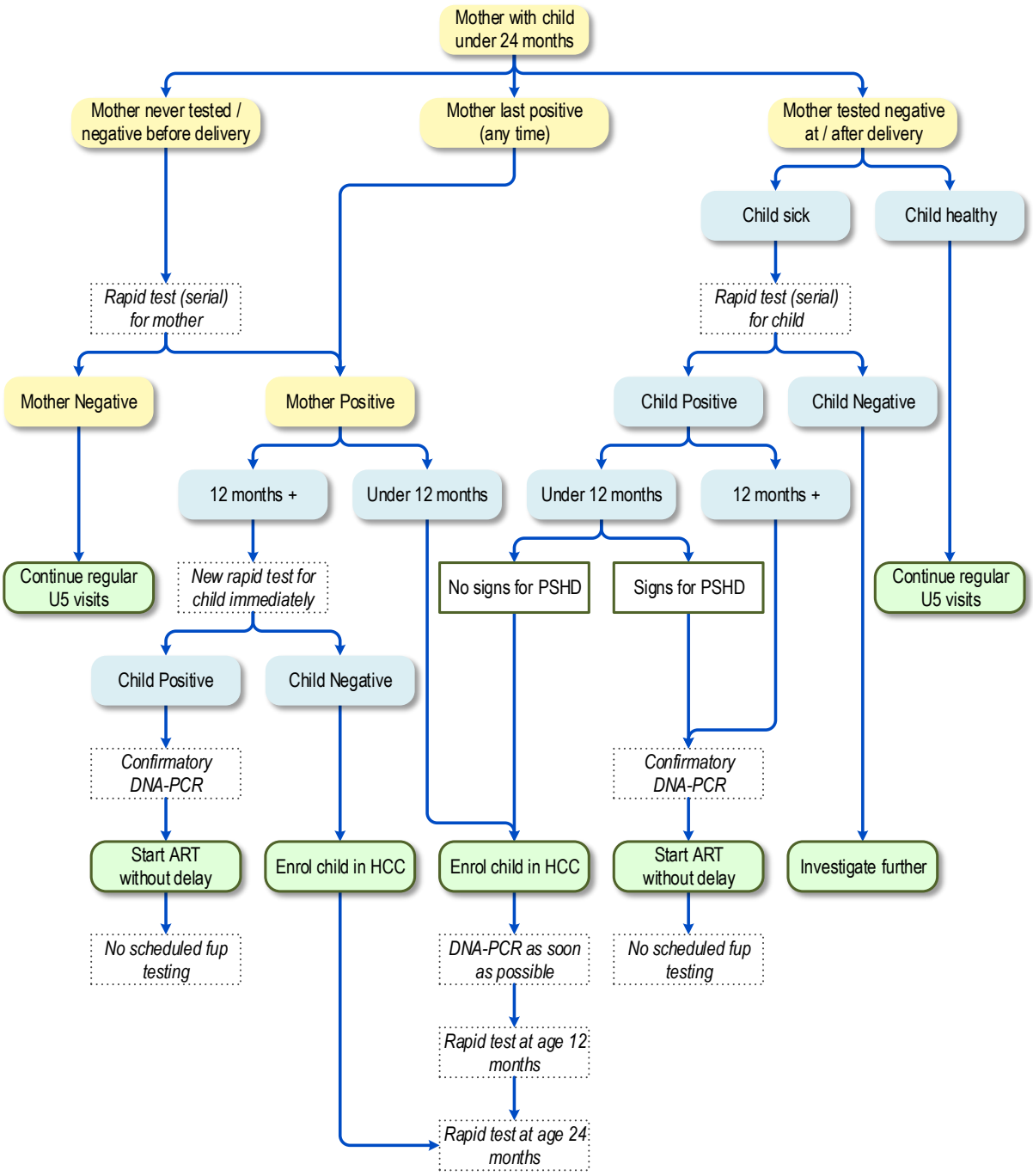


Table 3 on **page 18** shows the routine testing schedule for children under 2 years of age, the selection of the type of HIV test (DNA-PCR or rapid antibody test) depending on the child's age and the correct interpretation and action depending on the test result.

Table 3: Schedule of HIV testing in children: Choice of type of test, interpretation of results and follow-up management

Age (months)	Test	Schedule	Result	Interpretation	Action
Under 12	DNA-PCR (if available)	First opportunity from age 6 weeks	Negative	Not infected, but at risk of infection if breastfeeding	Continue HCC. Do rapid test at age 12 months.
			Positive	HIV infected	Start ART. Confirmatory DNA-PCR at ART initiation.
	Rapid antibody	Immediately if signs of PSHD identified ***OR*** If mother's HIV status cannot be ascertained	Negative	Not infected, but at risk of infection if breastfeeding from HIV+ mother	Treat condition. Continue HCC. Repeat rapid test at age 12 and 24 months.
			Positive	Possibly HIV infected if no PSHD symptoms	Enrol in HCC. Do DNA-PCR at first opportunity.
				Likely AIDS if symptoms for PSHD	Start ART. Confirmatory DNA-PCR at ART initiation.
12 to under 24	Rapid antibody	From age 12 months ***OR*** If mother's HIV status cannot be ascertained	Negative	Not infected, but at risk of infection if breastfeeding from HIV+ mother	Continue HCC, repeat rapid test at age 24 m.
			Positive	HIV Infected	Start ART. Confirmatory DNA-PCR at ART initiation.
24 and above	Rapid antibody	From age 24 months but ensure that BF stopped at least 6wks ago	Negative	Not infected	Discharge child from HCC.
			Positive	HIV Infected	Start ART. Confirmatory (parallel) rapid test at ART initiation.

6.3 Presumed severe HIV disease in infants (PSHD)

- Infants infected with HIV develop life-threatening HIV-related diseases much more quickly than older children and adults.
- It often takes too long to **confirm HIV infection** in a sick infant using **DNA-PCR**.
- Under the age of 12 months, a positive **HIV rapid antibody test does not confirm HIV infection** because maternal antibodies pass through the placenta and remain in the baby's blood for several months.
- However, a positive rapid antibody test in an infant with the following clinical signs makes **severe HIV disease** (AIDS) very likely:

Table 4: Definition of presumed severe HIV disease (PSHD)

Infant with positive rapid antibody test PLUS:		
Combination of 2:	**OR**	**At least 1:**
• Oral thrush • Severe pneumonia • Severe sepsis		• Severe unexplained wasting / malnutrition not responding to treatment • Pneumocystis pneumonia • Candidiasis of oesophagus, trachea, bronchi or lungs • Cryptococcal meningitis • Toxoplasmosis of the brain (from age 1 month)

- **Start ART** as quickly as possible for infants with PSHD – do not wait for a DNA-PCR result.
- Collect a DBS sample for DNA-PCR confirmatory testing on the day of starting ART (see **section 13.3** on **page 61**).

7 WHO Clinical Staging

Key Facts: WHO Clinical Staging

- Untreated HIV infection leads to a gradual destruction of the immune system.
- Different HIV-related diseases appear at different levels of immune suppression.
- Most of these diseases can also occur in HIV negative patients, but they are a lot more common and more severe in HIV infected patients.
- Actively search and treat HIV-related diseases at ART initiation and at every follow-up visit. ART alone may not save the patient.
- Patients may have several HIV-related diseases. Write all diseases found on the ART Patient Card.
- HIV-related diseases are grouped into 4 WHO clinical stages that correlate with disease progression and prognosis of survival:
    - Stage 1: Asymptomatic
    - Stage 2: Mild
    - Stage 3: Advanced
    - Stage 4: Severe
- Many patients have several HIV-related diseases from different stages.
    - List all conditions on the *ART Patient Card.*
    - The most severe condition determines the WHO clinical stage.
- Most WHO stage defining conditions apply to all ages, but some are only for children under 15 years and others are only for adults.
- WHO clinical staging requires confirmed HIV infection.
- An infant aged under 12 months with only a positive HIV rapid antibody test can NOT be given a WHO clinical stage because HIV antibodies in infants do not confirm HIV infection.
    - However, an infant with HIV antibodies and specific clinical conditions is very likely to have AIDS and needs to start ART without delay (see definition of *Presumed Severe HIV Disease* below).
- WHO clinical staging is mandatory for all HIV patients, regardless if a CD4 count is available.
- Keep blank (pre-) *ART Patient Cards* at OPD. Complete staging for every new HIV patient.

Table:5 WHO clinical staging for children and adults with confirmed HIV infection and definition of presumed severe HIV disease for infants

	Adults and Children	Adults only (15 years or older)	Children only (below 15 years)
1	• Asymptomatic • Persistent generalized lymphadenopathy		
2	• Respiratory tract infections, recurrent (sinusitis, tonsillitis, otitis media, pharyngitis) • Herpes zoster • Angular cheilitis • Oral ulcerations, recurrent • Papular pruritic eruptions / Fungal nail infections	• Moderate weight loss <10%, unexplained • Seborrhoeic dermatitis	• Hepatosplenomegaly, persistent unexplained • Lineal gingival erythema • Wart virus infection, extensive • Molluscum contagiosum, extensive • Parotid enlargement, persistent unexplained
3	• Fever, persistent unexplained, intermittent or constant, >1 month • Oral hairy leukoplakia • Pulmonary tuberculosis (current) • Tuberculosis (PTB or EPTB) within the last 2 years • Anaemia, unexplained < 8 g/dl • Neutropaenia, unexplained < 500 /mm^3 • Thrombocytopaenia, chronic < 50,000 /mm^3	• Severe weight loss >10% and/or BMI <18.5kg/m^2, unexplained • Diarrhoea, chronic (>1 month) unexplained • Oral candidiasis • Severe bacterial infections (pneumonia, empyema, pyomyositis, bone/joint, meningitis, bacteraemia) • Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis • Hepatitis B or C infection	• Moderate unexplained wasting / malnutrition not responding to treatment (weight-for-height/ -age 70-79% or MUAC 11-12cm) • Diarrhoea, persistent unexplained (14 days or more) • Oral candidiasis (from age 2 months) • Acute necrotizing ulcerative gingivitis or periodontitis • Lymph node tuberculosis • Bacterial pneumonia, severe recurrent • Symptomatic lymphoid interstitial pneumonitis • Chronic HIV-associated lung disease including brochiectasis
4	• Pneumocystis pneumonia • Candidiasis of oesophagus, trachea, bronchi or lungs • Extrapulmonary tuberculosis • Kaposi's sarcoma • HIV encephalopathy • Cryptococcal meningitis or other Extrapulmonary cryptococcosis • Disseminated non-tuberculous mycobacterial infection • Cryptosporidiosis, chronic with diarrhoea • Isosporiasis >1 month • Disseminated mycosis (coccidiomycosis or histoplasmosis) • Symptomatic HIV-associated nephropathy or cardiomyopathy • Progressive multifocal leukoencephalopathy • Cerebral or B-cell non-Hodgkin lymphoma	• HIV wasting syndrome (severe weight loss + persistent fever or severe weight loss + chronic diarrhoea) • Bacterial pneumonia, recurrent severe • Chronic herpes simplex infection (orolabial, genital / anorectal >1 month or visceral at any site) • Cytomegalovirus infection (retinitis or infection of other organs) • Toxoplasmosis of the brain • Non-typhoidal Salmonella bacteraemia, recurrent • Invasive cancer of cervix • Leishmaniasis, atypical disseminated	• Severe unexplained wasting / malnutrition not responding to treatment (weight-for-height/ -age <70% or MUAC <11cm or oedema) • Bacterial infections, severe recurrent (empyema, pyomyositis, bone/ joint, meningitis, but excluding pneumonia) • Chronic herpes simplex infection (orolabial or cutaneous >1 month or visceral at any site) • Cytomegalovirus infection: retinitis or other organ (from age 1 month) • Toxoplasmosis of the brain (from age 1 month) • Recto-vaginal fistula, HIV-associated **Presumed Severe HIV Disease in infants <12 months *(PSHD)*** Positive antibody (rapid) test *PLUS* one or several of the highlighted clinical conditions in the WHO staging list *OR* combination of at least 2 of the following: • Oral thrush • Severe sepsis • Severe pneumonia

8 HIV-related diseases

Key Facts: HIV-related diseases

- Use the following list to identify and manage the main HIV-related diseases seen in Malawi.
- A patient on ART who develops a new or worsening HIV-related disease may not be adherent and/or have drug-resistant HIV. Do a targeted VL after confirming good adherence in the last 3 months to rule out treatment failure. (see **section 15.10** on **page 77**)
- Tuberculosis (TB) and cryptococcal meningitis (CM) are responsible for a large proportion of AIDS deaths.
    - Many cases are never diagnosed / diagnosed and treated late.
    - Urine LAM (for disseminated TB) and CrAg (for CM using serum/plasma/full blood/CSF) tests are rapid, simple and cheap. A positive result is always indication to treat.

8.1 Routine urine LAM and serum CrAg screening

- Routinely test all **children 5 years+ and adults** with signs for advanced HIV:
    - **Urine LAM** for disseminated TB and
    - **CrAG** for cryptococcal meningitis (CM) / subclinical cryptococcaemia (serum or full blood).
- Eligible patient groups include:
    - CD4 < 200 cells/ml before ART initiation / while on ART. However, note that a CD4 test result is not required for urine LAM and CrAg if other criteria are met.
    - WHO stage 3 or 4 before ART initiation
    - "Seriously ill" PLHIV:
        - All PLHIV admitted as in-patient
        - HIV infected patients with any of the following danger signs:
        - **Adults:** ≥30 breaths/min; heart rate ≥120 beats/min; unable to walk unaided; ≥39°C
        - **Children**: lethargy; unconsciousness; convulsions; unable to drink or breastfeed; repeated vomiting; fever ≥39°C; tachycardia; tachypnoea
- Document LAM and CrAg screening results in patient health passport and on ART patient card.
- Urine LAM result
    - **Positive:** treat for TB, regardless of other TB diagnostics (see section 8.2.6 on page 24)
    - **Negative**: does not rule out TB. Continue with TB investigations according to TB guidelines.
- Serum CrAg
    - **Positive:** assess for active meningitis signs, treat for active meningitis or give pre-emptive antifungal therapy (see sections 8.2.1 and 8.2.2 on page 23).
    - **Negative:** does not rule out CM. Continue with CSF testing (CrAg, India ink, Xpert) and other investigations for patient with meningitis signs.

8.2 Management of HIV-related diseases

8.2.1 Cryptococcal meningitis

Clinical signs

Slow onset severe headache; confusion; convulsions; +/- fever; +/- neck stiffness

Diagnosis / investigations

Lumbar puncture (LP) feasible / not contraindicated

Cryptococcal antigen (CrAg) rapid test or India Ink stain on CSF.

LP not feasible

CrAg rapid test on serum, plasma or full blood.

Primary management

Admit

Daily therapeutic spinal tap if high intracranial pressure, severe headache or vomiting is present (up to 30 ml per puncture).

If not already on ART, start ART only 5 weeks after antifungal treatment initiation.

Induction phase

Do **not** give adjunctive corticosteroids during induction treatment

Option 1: Ampho B + Flucytosine for 7 days

Preferred option if both meds are available

Amphotericin B[2]

1mg/kg IV over 6 hours 24-hourly

Flucytosine tabs

100mg/kg/day divided into 4 doses (6-hourly)

Option 2: Fluconazole + Flucytosine for 14 days

This option requires FBC monitoring: at baseline and 2-3 times in the second week of treatment

Fluconazole tabs

Adult: 1200mg 24-hourly
Child: 12mg/kg (max 800mg) 24-hourly

Flucytosine tabs

100mg/kg/day divided into 4 doses (6-hourly)

Option 3: Ampho B + Fluconazole for 14 days

This option requires FBC, Crea and K+ monitoring: at baseline and 2-3 times in the second week of treatment

Amphotericin B[2]

1mg/kg IV over 6 hours 24-hourly

Fluconazole tabs

Adult: 1200mg 24-hourly
Child: 12mg/kg (max 800mg) 24-hourly

Consolidation phase

Fluconazole tabs for 8 weeks

Adult: 800mg 24-hourly
Child: 12mg/kg (max 800mg) 24-hourly

Maintenance phase

Fluconazole tabs, lifelong

Adult: 200mg 24-hourly
Child: 6mg/kg 24-hourly

8.2.2 Cryptococcaemia

Clinical signs

Often no clinical signs

Diagnosis / investigations

CrAg rapid test positive. Assess for meningitis signs. If positive, do full investigation and treatment for CM (see **section 8.2.1**)

Primary management

Fluconazole tablets

800 mg 24-hourly for 2 weeks *then*
400 mg 24-hourly for 8 weeks *then*
200mg 24-hourly for life

8.2.3 Toxoplasmosis

Clinical signs

New convulsions, possibly reduced consciousness, focal neurological symptoms

Only seen in patients with CD4 below 200 cells/ml

Primary management

Cotrimoxazole tablets 960 mg

4 tabs 12-hourly for 6 weeks **then**

[2] Before giving **Amphotericin B**: Pre-hydrate and supplement electrolytes: 1000ml NS + Potassium 2 tabs 12-hourly + Magnesium trisilicate 2 tabs 12-hourly.

Do not combine **Amphotericin B** with **TDF-based** ART (5A, 6A, 7A, 10A, 13A). Substitute for ABC-based regimen if already on ART. If not already on ART, start ART only 5 weeks after antifungal treatment initiation.

2 tabs 12-hourly for 3 months **then**
1 tab 12 hourly as lifelong prophylaxis

Response to this treatment in 7-10 days makes toxoplasmosis very likely

Secondary management

If cotrimoxazole is not tolerated

Clindamycin tablets
600mg 6-hourly for 3-6 weeks
+
Pyrimethamine tablets
100 mg 24-hourly for 3-6 weeks

8.2.4 Oral candidiasis

Clinical Signs

Multiple whitish or red patches anywhere inside mouth

Primary Management

Nystatin oral suspension
Treat for 7-14 days; keep in mouth as long as possible; apply to mother's nipples if breastfeeding
Adult: 4ml 6-hourly
Child: 1ml 6-hourly

Secondary Management

2 Alternative treatment options if severe or no response to nystatin:

Fluconazole tablets
Treat for 14 days
Adult: 100 mg 24-hourly
Child: 6mg/kg on day 1 then 3mg/kg daily

Miconazole gum patch or gel
Use for children > 4 months and adults
Treat with 1 patch 24-hourly for 14 days

8.2.5 Oesophageal candidiasis

Clinical signs

Retrosternal pain on swallowing; infants and children refusing to eat; +/- oral thrush

Primary management

Fluconazole tablets
Treat for 14 days
Adult: 200mg 24-hourly for 14 days
Child: 12mg/kg day one then 6mg/kg

8.2.6 TB

Clinical signs

Very variable depending on organs affected. Persistent fever / drenching night sweats; weight loss; failure to thrive; cough; anaemia <8g/dl; enlarged nodes; meningitis signs

Diagnosis / investigations

Often difficult to confirm in HIV+ patients. (Presumptive) TB case in household? 2x sputum for Xpert

Also consider for Xpert: ascites, CSF, lymph gland material, pleural or pericardial fluid

CXR; fine needle aspiration nodes (for microscopy); pleural tap for biochemistry: straw coloured effusion? Lumbar puncture: CSF for biochemistry, microscopy

Primary management

1st Line TB treatment
Don't delay empirical TB treatment in severely ill HIV patients with suspected TB

Category 1: New smear-positive or negative PTB:
Intensive phase: 2 RHZE
Continuation phase: 4 RH

Category 1: TB Meningitis:
Intensive phase: 2 SRHZ + predisolone
Continuation phase: 7 RH

Category 2: Relapse/ return after default/ treatment failure/ recurrent TB
Regimen according to drug-susceptibility testing.

Secondary management

MDR-TB
Specialised treatment (see NTP guidelines)

8.2.7 Pneumonia

Clinical signs

Productive cough; chest pain; fever; tachypnoea / dyspnoea

Diagnosis / investigations

Infiltrations on CXR

Primary management

Child:

Mild: Tachypnoea but no dyspnoea

(See IMCI guidelines)
Adult:

Mild to moderate presentation:

Amoxicillin tablets
500mg 8-hourly for 5 days
Doxycycline or Erythromycin if no response

Secondary management

Severe presentation:

Ceftriaxone 2g IV + macrolide or doxycycline
Add Gentamycin if no response

8.2.8 Pneumocystis carinii pneumonia (PCP)

Clinical signs

Extreme shortness of breath; dry cough; +/- fever

Severe pneumonia in infants <12 months

Diagnosis / investigations

O_2 saturation: hypoxia

CXR: Diffuse interstitial or hyperinflation; bats wing shadow

Treat empirically for PCP any HIV exposed or confirmed infected infant presenting with severe pneumonia.

Primary management

Admit
Oxygen
Cotrimoxazole tablets
Adult: 4 x 480mg 8-hourly for 21 days
Child: 80mg/kg 8-hourly for 21 days
Lifelong maintenance (CPT)
IV Cotrimoxazole if unable to swallow and NGT impossible to place
Prednisolone tablets:
Give only if patient is hypoxic / in respiratory distress.
Give 15-30 minutes before cotrimoxazole
Adult: 8 tablets 12-hourly for 5 days
8 tablet 24-hourly for 5 days
4 tablets 24-hourly for 11 days
Child: 2mg/kg 24-hourly for 7 days
1mg/kg 24-hourly for 7 days
0.5mg/kg 24-hourly for 7 days

Secondary management

Clindamycin
600mg 8-hourly for 3 weeks
plus
Primaquine
30mg 24-hourly for 3 weeks

8.2.9 Sepsis

Clinical signs

Severe illness; fever (can be absent, especially in children); fast heart rate; fast breathing

Diagnosis / investigations

+/- Malaria parasites; do not rule out sepsis if malaria parasites are seen; blood culture for culture and sensitivity (if available)

Primary management

Health Centre Level:

Immediate presumptive treatment
Referral to hospital

Child:

Benzyl Pen 50,000 IU/kg IV or IM stat +
Gentamycin 7.5mg/kg slow IV / IM stat +
Quinine 10mg/kg IM stat

Adult:

Chloramphenicol 1g IV or IM stat +
Gentamycin 240mg slow IV or IM stat +
Quinine 1200mg IV in 5% dextrose over 4 hours

Secondary management

Hospital management:

Neonate:

Benzyl Pen 50,000 IU/kg IV 8-hourly +
Gentamycin 7.5 mg/kg IV 24-hourly

Child:

Gentamicin 7.5.mg/kg 24-hourly + **Benzyl Pen** 50,000 IU/kg IV 8-hourly
OR
Ceftriaxone 50-100 mg/kg IV 24-hourly
OR (if pneumococcal sepsis suspected)
Chloramphenicol 25 mg/kg IV 8-hourly (max. 1g per dose)

When stable continue to complete 10 days:
Amoxicillin 40 mg/kg (total daily dose), divided into 3 doses given 8-hourly +
Ciprofloxacin 15 mg/kg 12-hourly

Adult:

Ceftriaxone 2g IV 24-hourly

When stable continue to complete 10 days:
Ciprofloxacin 750 mg tablets 12-hourly +
Amoxicillin 500 mg tablets 8-hourly

8.2.10 Kaposi sarcoma

Clinical signs

Single or multiple purple patches or nodes, mainly mouth, skin, conjunctiva, lung, GI tract; +/- enlarged lymph nodes; +/- oedema / pleural effusions

Children: often no skin lesions, only oedema and non-localized adenopathy.

Diagnosis / investigations

Usually clear picture; consider KS even without skin or oral lesions if no response to EPTB therapy within 4 weeks (adults).

Children: Look for woody oedema (hard, firm swelling) in the inguinal area / legs; facial oedema (rule out kidney disease, malnutrition); lesions in mouth / palate / subcutaneous.

Primary management

ART, analgesia, symptomatic treatment:
For all patients

Delayed chemotherapy:

For KS stage T0 (adults with only skin KS without oedema). Start chemotherapy only if no improvement after 3 months on ART.

Immediate chemotherapy:
For KS stage T1 (any paediatric KS and adult KS in mouth or internal organs, nodular skin KS, skin KS with oedema)

Chemotherapy 1st choice: paclitaxel IV

Paclitaxel vials must be refrigerated. Remainder can be kept in fridge for next dose.

Give Piriton tab 4mg 30-60 min before paclitaxel. Monitor for allergy / anaphylaxis (rare). Do not pre-medicate KS patients with corticosteroids.

Monitor FBC and LFT at baseline and before every paclitaxel infusion. Transfuse before paclitaxel if Hb<7g/dl.

Monitor clinically for hepatitis.

Dosing and administration
Dose is based on body surface area m^2 (BSA). Read BSA from **Figure 9** on **page 114** based on weight and height.

Dose can be rounded to nearest 5mg.

Dilute in 500ml NS, slow IV infusion. Wear protective gloves and gown when preparing.

Regimen 1: Medium dose paclitaxel

100mg/m^2 over 3 hours every 2 weeks. Usually 6-8 cycles. Continue until max. response, no active disease. Stop if severe side-effects.

Regimen 2: Low dose paclitaxel

25mg/m^2 over 1 hour weekly for 8 weeks. For very sick patients or those not tolerating Option 1.

Regimen 3: High dose paclitaxel

135mg/m^2 over 3 hours every 3 weeks. Continue until max. response, no active disease. Stop if severe side-effects. Alternative for patients in better condition who can only manage less frequent visits. Dose does not work well for many vial sizes.

Chemotherapy 2nd choice: bleomycin + vincristine

Ensure strictly IV injection as infiltration causes burns; document therapy and response in health passport; examine for recurrence at every visit.

Adult: 2 mg (1.5 mg/m^2) vincristine IV + 25 units (15 units/m^2) bleomycin IV

Child: 0.05 mg/kg vincristine IV (max 2mg) + 0.5 mg/kg bleomycin IM

Review after every cycle:
Severe neuropathy / constipation: stop vincristine
Sign for lung fibrosis (incl. cough, shortness of breath): stop bleomycin.
Cumulative max. life time dose for bleomycin is 400 units (maximum 16 doses)
Lesions cleared: stop treatment
Good response but residual lesions: continue next cycle
Poor response: Refer for secondary management.

Secondary management

Oncology department
Doxorubicin or other drugs may be used according to oncology protocols.

8.2.11 Lymphoma

Clinical Signs

Swollen lymph nodes, loss of weight, low-grade fever, night sweats, anaemia

Consider lymphoma if treatment for suspected lymph node TB shows no improvement after 4 weeks.

Management

Refer for lymph node biopsy, Management in Oncology department

8.2.12 Cervical (pre-) cancer

Clinical signs

Possibly vaginal discharge, but often no early symptoms.

HIV infected women are at high risk of cancer from human papilloma virus co-infection. Screen actively every 12-24 months.

Diagnosis / investigations

Acetic acid visualisation (VIA)

Use good light source.
Expose cervix with Cusco speculum.
Apply 4% acetic acid to cervix with large cotton swab for 2 minutes.
Inspect cervix.

Primary management

Depending on stage (see Cervical Cancer Screening Guidelines)
Pre-cancer
Cryotherapy or thermo-coagulation of pre-cancerous lesions can be done immediately after VIA.

Cervical cancer
Refer to tertiary care level for advanced treatment options or palliative care.

8.2.13 Herpes zoster (shingles)

Clinical signs

Grouped blisters in one patch; intense pain / burning; +/- fever; +/- body pains; lesions do not usually cross the body's mid-line

Primary management

Analgesic Ladder
Rigorous pain control
Acyclovir tablets
Must be started before blisters burst
Adult: 800mg 5 times per day for 7 days
Child: 20 mg/kg 8-hourly for 7 days
If face affected:

Refer to Eye specialist
Monitor for secondary bacterial infection

8.2.14 Seborrhoeic dermatitis

Clinical signs

Greasy, scaly rash in axilla, groin, scalp, neck, face

Primary management

Clotrimazole or Miconazole cream / ointment

Hydrocortisone 1% cream/ointment

Secondary management

Ketoconazole tablets
200 mg twice daily for 7 days
Flucloxacillin or Erythromycin
500mg 6-hourly for 7 days

8.2.15 Tinea corporis / cruris / pedis

Clinical signs

Round reddened plaques with scaly edge in multiple sites, poss. widespread

Primary management

Whitfield's ointment
Clotrimazole cream or Gentian-Violet paint
Apply twice daily for 3-4 weeks

Secondary management

Griseofulvin tablets
Adult: 500 mg 12-hourly for 4-6 weeks
Child: 20mg/kg per day for 4-6 weeks

8.2.16 Pruritic papular eruptions

Clinical signs

Severe itching, evenly distributed normal- or dark-coloured papules on trunk, arms or legs, often scratch-lesions

Primary management

Calamine Lotion
Antihistamines

Secondary management

Corticosteroid cream

8.2.17 Chronic diarrhoea

Clinical signs

More than 3 loose non-bloody motions per 24 hours for more than 4 weeks (adults) or 2 weeks (children)

Diagnosis / investigations

Based on response to stepwise empirical treatment:

Step 1 treats: isospora, cyclospora, bacterial

Step 2 treats: giardia, clostridium, amoeba, microsporidium

Step 3 treats: microsporidium, helminths

Primary management

Effective ART
Confirm VL suppression, do targeted CD4; consider if LPV/r is causing the diarrhoea.

ORS (Thanzi)
drink 5ml/kg 4-hourly and after every episode of diarrhoea.
drink 5ml doses every 5 min if vomiting occurs

IV Fluids
if severe de-hydration

Loperamide tablets
Adult: 2mg after every loose stool (max 12mg in 24 hours)
Child: Do NOT use for children

Step 1: Cotrimoxazole tablets
Adult: 960mg 8-hourly for 7 days
Child: 80 mg/kg 8-hourly for 7 days

Zinc tablets
Give for 10 days
Child 0-6mths: 10 mg 24-hourly
Child 6mths – 5 yrs: 20 mg 24-hourly

Secondary management

Continue with step 2 and 3 if no improvement

Step 2: Metronidazole tablets
Adult: 750mg 8-hourly for 7 days
Child: 15mg/kg 8-hourly for 7 days

Step 3: Albendazole tablets
Adult: 400mg 12-hourly for 6 months

8.2.18 Genital ulcer disease

Clinical signs

Skin ulcer and/or blisters on genitals with or without pain

Diagnosis / investigations

History, examination

Primary management

Emphasize importance of completing treatment

Avoid sex without condom until treatment complete, give min. 30 condoms

Give referral slip to treat partner

Benzathine Penicillin
2.4 Million Units IM stat

Ciprofloxacin tablets
500 mg 12-hourly for 3 days

Acyclovir tablets
800 mg 8-hourly for 2 days

8.2.19 Urethral discharge

Clinical signs

Turbid discharge from urethra, usually with pain when passing urine

Diagnosis / investigations

History, examination

Primary management

Emphasize importance of completing treatment

Avoid sex without condom until treatment complete, give min. 30 condoms

Give referral slip to treat partner

Gentamicin 240 mg IM stat

Doxycycline tabs 100 mg 12-hourly for 7 days

Metronidazole tabs 2 g stat

8.2.20 Abnormal vaginal discharge

Clinical signs

Vaginal discharge, unusual colour / odour

Itching, pain / discomfort, pain when passing urine

Diagnosis / investigations

History, examination

Primary management

Emphasize importance of completing treatment

Avoid sex without condom until treatment complete, give min. 30 condoms

Give referral slip to treat partner

Gentamicin 240 mg IM single dose

Doxycycline tabs 100 mg 12-hourly for 7 days

In pregnancy: **Erythromycin tabs** 500 mg 6-hourly for 7 days

Metronidazole tabs 2g stat

8.2.21 Lower abdominal pain (Women, STI)

Clinical signs

Pain during sexual intercourse/ when passing urine/ around menses

Vaginal discharge / excessive bleeding at / between periods

Fever / nausea / vomiting

Diagnosis / investigations

History, examination

Primary management

Emphasize importance of completing treatment

Avoid sex without condom until treatment complete, give min. 30 condoms

Give referral slip to treat partner

Gentamicin 240 mg IM stat

Doxycycline tabs 100 mg 12-hourly for 14 days

Metronidazole tabs 400 mg 12-hourly for 14 days

9 Standard monitoring of HIV patients

Key Facts: Clinical monitoring

- Exposed children and ART patients need the same standard clinical assessment at every clinical visit.
- Check actively – do not rely on patients to report problems unprompted.
- The Standard Clinical Monitoring Checklist (Table 7 on Page 33) helps to find:
  - HIV-related diseases
  - ART failure
  - Drug side effects (ART, TB, CPT, IPT, etc.)
- It can be difficult to distinguish HIV-related diseases from side effects. An ambiguous symptom is likely a side-effect if it started / worsened after starting medication / improves after stopping.

9.1 Monitoring of nutritional status

- One of the simplest methods to detect HIV disease progression / ART failure.
- Investigate any patient with weight loss for TB
- Record length / height to the nearest cm at every visit (children) / once at enrolment (adults).
- Record weight in kg to the nearest 100g at every visit (children and adults).
- Use appropriate nutrition indicator for children and adults.

9.1.1 Children 0-14 years

- Classify and manage wasting / malnutrition status according to ***Malawi Guidelines for Community Management of Acute Malnutrition (CMAM)***.
- Watch out for flattening of the growth curve (weight for age).

9.1.2 Non-pregnant adults 15 years and above

- Classify nutrition status according to BMI. Use standard MOH job-aids.
- Watch out for any weight loss over time. Review documented previous weight whenever available as reported weight loss can be unreliable.
- BMI under 17: Start TF for ‘moderate malnutrition’.
- BMI under 16: Start TF for ‘severe malnutrition’.

9.1.3 Pregnant and lactating women

- Use MUAC instead of BMI.
- MUAC less than 22cm: start TF for ‘moderate malnutrition’.
- MUAC less than 19cm: start TF for ‘severe malnutrition’.

9.2 Standard clinical monitoring checklist

- Use the summary clinical monitoring checklist to actively screen every exposed child and ART patient for clinical symptoms at every clinical visit.
- Refer to **Table 7** on page 33 for more detailed screening instructions and interpretation of signs and symptoms for further management.

Table 6: Checklist for clinical monitoring of HIV exp. children and ART patients

Ask for / Examine			
Appearance:	Weight loss / failure to thrive	N	Y
	Body shape change / breast swelling (men)	N	Y
	Swollen glands	N	Y
Headache / confusion / dizziness		N	Y
Yellow eyes		N	Y
Mouth sores		N	Y
Cough		N	Y
Shortness of breath		N	Y
Fever / night sweats		N	Y
Vomiting / abdominal pain		N	Y
Diarrhoea		N	Y
Leg pain / numbness / weakness		N	Y
Rash on arms, legs or trunk		N	Y

Table 7: Detailed clinical monitoring list for HIV exp. and ART patients

Ask / Examine	Look for	Assess	Disease (most common)	Drug Side-Effects
Appearance	• Weight loss • Failure to thrive	• Weight loss: trend from patient card / health passport • BMI (adults) • Weight for height, weight for age, MUAC (children)	1) TB 2) Chronic diarrhoea 3) Malnutrition 4) ART treatment failure 5) Malignancy (lymphoma)	**Lactic acidosis due to ART** 1) AZT
	• Breast swelling (men) • Body shape change	• Breast enlargement (gynaecomastia) • Slimming of cheeks • Slimming of forearms, buttocks and legs +/- protruding veins • Fattening of chest / belly / buttocks • Buffalo hump		**Gynaecomastia** 1) EFV **ART induced lipodystrophy** 1) AZT 2) 3TC
	Swollen glands	• Cervical / axillary lymphadenopathy	1) PGL 2) EPTB 3) Lymphoma 4) KS (+/- skin lesions) 5) BCG adenitis	
Headache, confusion, dizziness	• Neck stiffness • Nausea / vomiting		1) Meningitis (bacterial/ TB, cryptococcal) 2) Toxoplasmosis HIV dementia	1) EFV 2) INH 3) DTG

Ask / Examine	Look for	Assess	Disease (most common)	Drug Side-Effects
Yellow eyes	• Yellow sclera	• Jaundice	1) Viral hepatitis 2) Alcoholic hepatitis 3) Malaria 4) Cancer 5) Hep B-IRIS	**Drug hepatitis** 1) NVP 2) EFV 3) PZA 4) Rifampicin 5) INH 6) Fluconazole 7) DRV/r 8) ETV 9) DTG **Hyperbilirubinaemia** 7) ATV/r
Mouth sores	• Mucosa lesions	• Whitish patches • Painful red patches	1) Oral thrush 2) Oral hairy leukoplakia	
		• Purple lesions	1) KS	
		• Ulcerations	1) Acute ulcerative stomatitis/ gingivitis/ periodontitis 2) Herpes simplex 3) Angular cheilitis 4) Aphthous ulcers	**Hypersensitivity** 1) ABC 2) NVP 3) EFV 4) ETV 5) Cotrimoxazole
Cough	• Duration • Productiveness	• Less than 2 weeks • Fever • +/- Productive	1) Pneumonia (bacterial) 2) TB suspect: circle on card 3) PCP	**Hypersensitivity** 1) ABC 2) DRV/r 3) ETV
		• More than 2 weeks • Fever / night sweats	1) TB suspect: circle on card 2) KS	

Ask / Examine	Look for	Assess	Disease (most common)	Drug Side-Effects
Shortness of breath	• Observe breathing • Pleural effusion	• Pleural effusion	1) EPTB 2) Bacterial pneumonia 3) Heart failure 4) KS	
		• No pleural effusion	1) Bacterial pneumonia 2) PCP 3) TB +/- pneumothorax	**Lactic acidosis due to ART** 1) AZT
	• Conjunctiva	• Pale conjunctiva	1) HIV anaemia 2) Chronic severe malaria 3) Nutritional anaemia	**Anaemia** 1) AZT
Fever / night sweats	• History / Duration • Current temperature	• Less than 1 month	1) URTI / viral 2) Sepsis 3) Malaria 4) TB	**Hypersensitivity** 1) ABC 2) NVP 3) EFV 4) RAL 5) ETV 6) DTG 7) Cotrimoxazole
		• More than 1 month	1) TB 2) Malignancies (lymphomas)	
Vomiting / abdominal pain	• Hydration status • Palpate abdomen	• Dehydration • Tenderness	1) TB 2) NTS sepsis 3) Acute Gastro-enteritis 4) Malaria 5) Abdominal TB 6) Ulcer disease 7) CNS disease 8) Hepatoma	**Drug-induced pancreatitis** 1) 3TC 2) RAL 3) ETV 4) DTG **Lactic acidosis due to ART** 1) AZT

Ask / Examine	Look for	Assess	Disease (most common)	Drug Side-Effects
Diarrhoea	• History • Blood in stool	• Less than 1 month	1) Salmonella E. Coli Amoeba, Shigella 2) HIV / OI	**GI toxicity** 1) LPV/r 2) NVP 3) AZT 4) ABC 5) 3TC 6) DTG Antibiotics: Pseudomembranous enterocolitis
		• Longer than 1 month	1) HIV / OI 2) Abdominal TB	
Leg pain, numbness, weakness	• History • Neurological exam	• Sleep disturbance (moderate) • Motor involvement (severe)	1) HIV peripheral neuropathy 2) spinal TB	**Drug neuropathy** 1) INH 2) AZT 3) Vincristine 4) Metronidazole
Rash on arms, legs and trunk	• Skin lesions	• Purple lesions	1) KS	
		• Blisters/ vesicles	1) Shingles/ varicella zoster	Stevens-Johnson Syndrome 1) NVP 2) Cotrimoxazole 3) RAL
	• Generalized rash	• Maculo-papular	1) HIV associated rash (PPE) 2) Fungal skin infections 3) Molluscum contagiosum 4) Scabies	**Skin toxicity** 1) NVP 2) EFV 3) CTX 4) Fluconazole 5) DRV/r 6) ETV 7) DTG

9.3 CD4 count testing

Key Facts: CD4 count testing

- About 30% of patients have a CD4 count <200 cells/ml at the time of starting ART and are therefore at high risk of TB, CM and other HIV-related diseases.
- Do **routine CD4 count** and start ART if a CD4 machine is available at the site. However, do not delay ART initiation if CD4 machine is down / results are delayed or testing is currently not available.
- Do **Targeted CD4 count** for patients with suspected clinical and/or confirmed treatment failure (VL).
    - CD4 <200 cells/ml: Do routine urine LAM and serum CrAg (see **section 8.1** on **page 22**).
    - CD4 200+ cells/ml: no specific action
- CD4 counts are the most direct routine measure for HIV immune suppression, but can be influenced by several factors:
    - Gender, time of day, physical exercise, pregnancy, smoking, etc.
- CD4 counts may fail or give wrong results unless the following protocol is used:
    - Collect a minimum of 2ml venous blood in tube with EDTA anticoagulant.
    - Immediately turn the tube upside down to mix the blood with EDTA. Do not shake vigorously
    - The sample must be processed in the lab within 6 hours or 48 hours, depending on the type of machine used.
    - Storing the tube at 2-8° C in the dark will extend the lifespan by a few hours
    - Protect the tube from hard vibrations during transport.

9.4 Collection of DBS samples for EID and VL

Key Facts: EID and VL testing

- Diagnosing HIV infection in infants and detecting treatment failure in patients on ART is done by testing for HIV genetic material in a blood sample.
- This requires making millions of copies of the genetic material so that there is enough to be measured. This method is called polymerase chain reaction (PCR). PCR is very sensitive and it can be disturbed by tiny amounts of dirt or contact with other samples.
- PCR testing is only done in special labs, making it necessary to prepare dried blood spot (DBS) samples that can be kept at normal temperature for several weeks.
- Carefully follow the protocol when preparing DBS samples. Most steps are the same, but there are some **important differences between** DBS for **EID** and **VL** (shown below).
- **Never** allow EID samples to **touch or mix** with VL samples as this will lead to false positive EID results:
    - Use separate rooms or at least separate tables within one room.
    - Allocate different staff for collection of DBS for EID and VL.
    - Use separate drying racks, clearly labelled ***EID*** and ***VL.***
- Pack DBS for EID and VL in separate plastic bags and envelopes.

Table 8: Summary protocol for preparation of DBS samples for EID and VL

	Early Infant Diagnosis (EID)	Viral Load (VL)	Caution
Getting ready	• Label DBS card with patient name, ID and date • Wash hands, put on gloves, wash powder off gloves (unless powder-free)		• Hold the filter paper card only at the edges • Never touch the area near the circles
Sample collection	• Infants <9kg: select left or right side of the sole under the heel • Children under 2 years >9kg: select heel or side of big toe • From age 2 years and adults: select side of fingertip, preferably ring finger • Position down, warm up, squeeze intermittently		
	• Wipe with alcohol swab, dry for 30 sec • Press lancet on skin, prick, dispose into sharps bin • Wipe away first drop of blood with sterile gauze, wait for large drop of blood to appear		• Avoid excessive squeezing of heel / toe / finger
	• Drip one free drop of blood directly onto filter paper	• Dip capillary into blood drop and fill to black line (50 micro litres) • Hold tip of the capillary at a slight angle in the centre of the circle on the filter paper	• Don't allow the finger / toe to touch the filter paper • Apply blood only on one side of filter paper • Don't rub or scratch filter paper with capillary
	• Let the blood soak into the paper to fill the whole circle • Repeat this procedure until all **5 circles** are filled		• Don't re-apply more blood to the same circle
Drying	• Slot filter paper into drying rack • Dry in protected area at room temperature for at least 3 hours (best overnight)		• Don't touch/ smear/ allow to touch other objects • Protect from sunlight, heat, dust, insects, rodents
Packing	• Put each filter paper card into a separate zip-lock bag • Put 3 sachets with desiccant into each zip-lock bag • Squeeze out air and seal zip-lock bag • Use marker pen to label the zip-lock bag and envelope, including **'EID'** or **'VL'** • Insert zip-lock bags and specimen forms in this envelope and seal		• Don't pack filter paper cards before completely dried • Don't combine EID and VL samples in same envelope
Storage, transport	• Store envelopes in cool dry place		• Keep away from sunlight

10 Preventive services for HIV patients

Key Facts: Preventive services

- A simple standard package of preventive services is provided for all ART patients. This includes:
    1. Provider Initiated Family Planning (at least condoms + Depo-Provera)
    2. Cotrimoxazole Preventive Therapy
    3. Isoniazid Preventive Therapy (in districts with high TB burden)
    4. Insecticide Treated bed Nets
- This package effectively reduces:
    - HIV transmission to sexual partners
    - HIV transmission from mother to child by preventing unwanted pregnancies
- Serious HIV-related diseases (TB, diarrhoea, pneumonia, malaria, etc.)

10.1 Provider initiated family planning (PIFP)

Key Facts: Family planning

- Avoid unwanted pregnancies, regardless of HIV infection status.
- Use 'dual protection' – condoms alone are not enough for family planning as they have to be used very consistently.
- Sex without condom is risky if the infected partner's viral load is not suppressed. Consistent condom use is especially important in the first 6 months after starting ART and/or if viral suppression is not confirmed (e.g. low adherence and/or treatment failure).
- Some hormonal contraceptives (the pill and implants) may be less effective with ARVs or TB treatment because of drug interactions.
- Depo-Provera does not interact with ARVs or TB drugs, but it is generally slightly less effective in preventing pregnancy than implants.
- Intrauterine device, vasectomy and tubal ligation are safe to use with ART.
- Encourage HIV positive women to make an informed choice about pregnancy. Health workers should not actively discourage pregnancy as the risk of transmitting HIV to the baby is less than 5% if the mother :
    - Starts ART as early as possible, best before conception
    - Is fully adherent to ART throughout pregnancy and breastfeeding

Implementing routine PIFP in HIV clinics

- Assume that all patients aged 15 years and above are sexually active.
- Offer condoms to all men and women age 15 years and above:
    - Minimum of **30** male and/or female condoms
- Offer counselling on contraceptive methods. Refer to FP clinic if this is not feasible in the HCC setting.
- Offer at least Depo-Provera directly in the HCC (one-stop shop)
    - 1 Depo-Provera injection every 3 months
- Give patients the opportunity to refuse either method if they feel they don't need / want it.

10.2 Cotrimoxazole preventive therapy (CPT)

Key Facts: CPT

- CPT prevents PCP pneumonia, diarrhoea, malaria and other HIV-related diseases and prolongs survival.
- Start all of the following on CPT:
    - HIV exposed children from age 6 weeks
    - HIV infected children from age 6 weeks
    - HIV infected adults
- Continue CPT for life for all HIV positive patients.
- Stop CPT in HIV exposed children when confirmed negative after stopping of breastfeeding (when discharged from exposed infant follow-up).
- Provide CPT to all patients in HCC and ART follow-up.
- CPT is tolerated very well by most patients, can be taken at the same time with ART, TB treatment and IPT.
- CPT is safe in pregnancy.
- Do not combine CPT with SP – HIV positive pregnant women only take CPT (and ART).
- Children from 30.0kg and adults take one 960mg tablet of cotrimoxazole 24-hourly.
- Dispersible paediatric tablets (120mg) are used for children under 14.0kg. Dosing of paediatric CPT and ART are both based on the same weight bands.
- CPT 960mg is usually available in blister-packs of 10 tablets – 3 strips are for a 30 day supply.
- Poor adherence to CPT is a warning sign for poor adherence to ART.

Eligibility for CPT

- All infants born to HIV infected mothers (without confirmed HIV infection) from age 6 weeks:
    - Aim to start CPT straight after the infant has finished NVP syrup.
    - Note: start HIV-exposed infants on CPT even if they did not receive NVP prophylaxis.
    - Keep the infant on CPT until s/he is confirmed HIV-negative and is discharged from HCC follow-up (around age 24 months).
- Confirmed HIV infected children from age 6 weeks and adults:
    - No contra-indication against CPT in the first trimester of pregnancy.
    - Do not give SP to HIV infected pregnant women on CPT.
    - If SP has already been taken, wait for 14 days before starting CPT.

CPT contraindications

- Jaundice
- Renal failure
- Suspected allergy to any of the following sulphonamide drugs (skin rash, mucosal ulceration, severe anaemia, leukopenia)
    - Cotrimoxazole
    - Sulfadoxine / Pyrimethamine (SP)

CPT dosage and duration

- See **Table 12** on page **54** for dosing.
- HIV exposed children: stop CPT when confirmed HIV negative at least 6 weeks after stopping of breastfeeding.
- HIV infected children and adults continue CPT for life, unless severe side effects develop.
- Poor adherence to CPT will reduce the effectiveness of preventing HIV-related diseases, but it is less risky than poor adherence to ART.

10.3 Isoniazid preventive therapy (IPT)

Key Facts: IPT

- Daily IPT can prevent active TB disease in people who are at high risk.
- Give IPT to the following:
    - HIV infected children and adults in the 5 high burden districts (see below), regardless of TST status (if known). Continue IPT for life for all patients on ART in the 5 districts.
    - Children under 5 years – regardless of HIV status - who live with a patient with pulmonary TB (sputum smear negative or positive; in all districts). Give 6 months course of IPT.
- Do not give IPT to a patient who has any signs suggestive of active TB: such patients need full investigation for TB and combination TB treatment if confirmed to avoid TB drug resistance.
- Over half of all new TB cases in Malawi come from **5 high burden districts**:
    - Lilongwe, Blantyre, Zomba, Thyolo, Chiradzulu.
    - In these districts, IPT **benefits** are more likely to **outweigh** the **risk** of side effects (see below).
- In the 5 high burden districts:
    - New patients: start IPT together with ART and CPT.
    - Patients already on ART: start IPT regardless of the time on ART.
    - Give IPT regardless of previous TB treatment or prior use of IPT.
    - Continue IPT for life as long as the patients remains in a high burden district.
- IPT can be taken in pregnancy and combined with CPT and ART.
- IPT is well tolerated by over 95% of patients and most side effects are mild and disappear within the first 3 months.
- Serious side effects are uncommon: hypersensitivity, neuropathy and severe hepatitis.
- Stop IPT if any of the following are seen:
    - Vomiting
    - Pellagra-type skin rash in sun-exposed areas and other severe skin rash
    - Yellow eyes
    - Dizziness / confusion / convulsions
    - Severe numbness/burning pain and muscular weakness of legs and/or arms
- Document reason for stopping IPT in patient health passport.

Eligibility for IPT

- Patients on ART in one of the 5 high burden districts.
- Rule out active TB with the standard screening questions below:
  - Current cough: any duration, productive or non-productive
  - Unexplained weight loss (adults)
  - Failure to thrive and/or malnutrition (children)
  - Fever and/or night sweat

IPT contraindications

- Suspected or confirmed active TB
- Active hepatitis, liver damage, heavy alcohol drinking
- Severe peripheral neuropathy

IPT dosage and duration

- See **Table 12** on page **54** for dosing.
- Give IPT during ART visits. One extra visit is needed 1 month after starting IPT.
- Review patients at month **1**, **3** and **6** after starting IPT for any side-effects.
  - IPT initiation: Give INH and pyridoxine for 1 month.
  - 1 Month IPT review: Give INH and pyridoxine for 2 months.
  - From 3 Month IPT review: Continue giving INH and pyridoxine for 3 months.
- Give 1 tablet of pyridoxine 25 or 50mg 24-hourly to children and adults.
- Continue **IPT for life** as long as the patient remains in ART care in one of the **5 high TB burden** districts.
- Stop / interrupt IPT if a patient transfers (permanently) to an ART clinic in a non-high TB burden district. Re-start IPT if the patient transfers back into a high TB burden district.
- Poor adherence to IPT will reduce the effectiveness of preventing active TB disease, but it will not cause drug-resistant TB.

10.4 Insecticide treated bed nets (ITN)

- Dispense 1 ITN to each patient at enrolment into HIV Care.
- Dispense 1 replacement ITN every 2 years and document this on the ART patient card.

11 Understanding ART regimens and formulations

Key Facts: ART regimens

- ART requires combining **3 different ARVs** that act differently to avoid development of drug-resistant HIV.
- Use only the standard ARV regimens for the specified patient groups shown in these guidelines. Other ARV combinations may cause more side effects or lead to drug-resistant HIV. Non-standard (NS) regimens can only be prescribed by specialists for complicated cases.
- Do not change ART regimens without a clear indication. Unnecessary regimen changes spoil future treatment options.
- **1st Line regimens** are the best. Patients can remain on the same 1st line regimen possibly for life if they are fully adherent. All 1st line regimens:
    - Are easy to prescribe and easy to take.
    - Have a low risk of serious side effects and require no lab monitoring for toxicity.
    - There are **7 different 1st line** regimens:
    - **4** are standard for **initiating ART** depending on patient age and weight (see Table 11 on Page 52). Three of these are fixed-dose combinations: only 1 type of tablet is taken.
    - Move all patients with significant side effects to an alternative regimen without delay. Chose the regimen by **substituting** only the ARV responsible for the side effects.
    - All children started on Regimen **2P** start using adult formulation (**2A**) from 25kg. Routinely change all boys to regimen **13A** and all girls to **5A** once they have reached 30kg. Regimen 13A has important advantages for adolescents (see **page 46**).
- **2nd Line regimens** are a lifeline for patients who have confirmed treatment failure on 1st line regimen (usually due to poor adherence in the past). Moving from 1st to 2nd line ART is called **switching**. 2nd line regimens:
    - Contain a completely different class of ARVs (protease inhibitors)
    - Are more complicated to prescribe and take
    - Can have more side effects
    - There are **5 different 2nd line** regimens. The appropriate 2nd line regimen is determined by the 1st line regimen that the patient was taking when failing.
    - Children **under 3 years** may respond better when **started immediately on a 2nd line** regimen. Specialized sites that can ensure extra support with giving a more complex regimen to small children should routinely initiate children under 3 years on 2nd line ART (see details on **page 50**).
- **3rd Line regimen** is a last resort for patients failing on second line. This requires confirmation of drug resistant virus using genetic analysis in the lab. 3rd line can only be initiated by a specialised ARV clinician upon authorization of the 3rd line review committee.
    - Very expensive
    - Can have more side effects and is more difficult to take.

Key Facts: Dolutegravir (DTG)

- DTG-based ART regimens (**13A**, **14A, 15A**) have **important advantages**
  - More potent: rapid viral load suppression within weeks
  - More durable: high drug-resistance barrier
  - Convenient: small tablet taken once per day
  - Better tolerated: very few patients experience significant side effects
  - Fewer drug-interactions (see below): no interactions with hormonal contraceptives
- **(Relative) Contra-indications** for DTG-based regimens:
  - It is currently not confirmed that DTG is safe in early pregnancy and it is therefore not used in standard 1st line for girls/ women who may get pregnant while on ART.
  - Uncontrolled diabetes
  - Renal failure: creatinine clearance <30ml/min
  - Severe liver damage: ascites; albumin <2.8g/dL; total bilirubin >50mmol/L; encephalopathy
- Potential **side-effects** (rare):
  - Insomnia, headache, agitation
  - Nausea, diarrhoea
  - Skin rash
- Potential **risks**
  - Delay ART initiation by 5 weeks for patients treated for cryptococcal or TB meningitis (see **section 8.2.1** on **page 23**) due to the risk of IRIS (see **section 15.12** on **page 86**).
- Important DTG **drug-interactions**:
  - Rifampicin (TB treatment): double daily DTG-dose (see **section 14** on **page 68**).
  - Drugs with iron, magnesium, calcium, zinc (FeFo, multi-vitamins, antacids, etc.): take 2 hours before or 6 hours after DTG
  - Metformin (diabetes): limit daily dose to 1000mg, confirm effective glucose control
  - NVP, ETR (ARVs): do not combine with DTG
  - Carbamazepine, phenytoin, phenobarbitone: do not combine with DTG
- DTG may be used in 1st, 2nd and 3rd line ART regimens
  - DTG remains effective for patients who have failed on other 1st and 2nd line regimens.
  - However, it is not yet known if DTG-based 2nd line is a good option for patients with extensive resistance.

11.1 Classification of individual ARVs

- Main classification is based on **mode of action** against HIV replication.
- Sub-classification is based on **biochemical structure** of the drug.
- Only ARVs with the same dosing interval are available as fixed-dose combinations.

Table 9: Classification of ARVs

Mode of action	Biochem. structure	Abbrev.	ARVs	Dosing interval
Reverse **T**ranscriptase **I**nhibitors	**N**ucleosides	***NRTI***	**AZT**	***12**-hourly*
			3TC, ABC	***12**- or **24**-hourly*
			TDF	***24**-hourly*
	Non-**N**ucleosides	***NNRTI***	**NVP**	***12**-hourly*
			EFV	***24**-hourly*
			ETV	***12**-hourly*
Protease **I**nhibitors		***PI***	**ATV/r**	***24**-hourly*
			DRV	***12**-hourly*
			LPV/r	***12**-hourly*
Integrase **S**trand **T**ransfer **I**nhibitor		***INSTI***	**DTG**	***24**-hourly*
			RAL	***12**-hourly*

11.2 Choosing ART regimen, formulation and dosage

11.2.1 Regimen names

- **Table 11** shows the standard ART regimens for Malawi.
- Regimens are numbered for ease of reference:
  - Regimen 0, 2, 4, 5, 6, 13, 14 and 15 are 1st line regimens, including alternative 1st line regimens.
  - **Regimen 5** is the standard 1st line for girls/women who may get pregnant while on ART.
  - **Regimen 13** is the new standard 1st line regimen for males weighing 30kg or above and women aged 45 years or above.[3]
  - Regimen 1 and 3 contain stavudine (d4T). They are no longer used and have been deleted.
  - Regimen 7 – 11 are 2nd line regimens.
  - Regimen 12 is the standard 3rd line regimen.
  - An "**A**" is added to the regimen number for adult formulations (e.g. Regimen 2A) and a "**P**" is added for paediatric formulations (e.g. Regimen 2P).

[3] Regimen 13, 14 and 15 can also be used for women if reliable contraception can be assured.

- Fixed dose combinations (FDC) are shown with a slash (e.g. TDF **/** 3TC **/** DTG).
- Combinations made up of separate tablets are shown with + (e.g. AZT/3TC **+** EFV).
- **3TC (lamivudine)** is the backbone in **ALL** 1st and 2nd line regimens because it is extremely well tolerated and remains active even when drug-resistant HIV is present.

11.2.2 Paediatric / adult formulations

- Most regimens are suitable for children and adults and are available as both adult and paediatric strength tablets, but:
    - TDF may affect growing bones and is not given to children under 2 years. The standard adult formulation (TDF 300mg) can be used from 30kg.

11.2.3 Start regimen

- Select one of 4 standard regimens to start patients on ART, based on age, weight and sex

Table 10: Selection of ART regimen for initiation

Age (years)	Weight (kg)	Sex	Conditions	Regimen
Under 3 year	-	-	No extra support	**2P**
			Extra treatment support available	**11P**
3 years or above	Under 25kg	-		**2P**
	25 - 29.9kg	-		**2A**
	30kg +	Male		**13A**
		Female	May get pregnant while on ART	**5A**
			On permanent contraception / 45 years +	**13A**

- Start children under 3 years on regimen **11** if the site can ensure extra support with giving a more complex regimen to small children (see **section 11.2.11** on **page 50**). Use regimen 2 otherwise.
- Use alternative 1st line regimens if the patient has any contraindications for the standard regimen.

11.2.4 Initial prescriber level

- All MOH-certified PMTCT/ART providers are authorized to start any of the seven 1st line regimens, but only experienced ART staff (certified Level 2 providers) are authorized to initiate 2nd line regimens.
- However, follow-up prescriptions for 2nd and 3rd line regimens can also be made by Level 1 providers. See details in **section 11.3** on **page 55**.

11.2.5 'Starter pack'

- Regimens with NVP (regimens **0, 2** and **6**) need to be *phased in* to avoid potentially severe hepatitis or skin toxicity. During the first 2 weeks, the NVP-containing FDC is taken only once daily (before bed). The other 2 ARVs are taken in the morning to achieve 12-hourly dosing from the first day.

- *Starter packs* are dispensed as a 2-week supply of one pack of the triple ARV fixed-dose combination (with NVP) plus one pack of the other 2 ARVs in combination (without NVP). Dispense the required number of tablets in labelled tablet dispensing bags.
- *Starter packs* are needed for all patients starting Regimen **0, 2** or **6:**
    - For the **first time** (new ART initiation)
    - After interrupting ART for more than **14 days** (re-initiation / re-start)
- *Starter packs* are **NOT** given when changing without interruption from an EFV-containing regimen (4 or 5) to regimen 0, 2 or 6. This is because patients on EFV already excrete NVP faster.

11.2.6 'Tail' needed

- NVP and EFV remain in the body much longer than the other ARVs. Stopping any 1st line regimen due to side-effects (or due to patient's decision, etc.) therefore requires giving a 7-day '*tail*' of the other 2 ARVs in the regimen to avoid exposing the virus to only NVP or EFV, which would risk development of NVP- and EFV-resistant HIV and spoil future treatment options.
- However, do **NOT** give a *tail* in case of severe potentially life-threatening side effects caused by NRTIs (lactic acidosis, pancreatitis), but stop all ARVs immediately.

11.2.7 Contraindications

- Most contraindications are not absolute for a specific regimen: balance risks, benefits and alternatives. Usually, a suitable alternative regimen can be chosen from **Table 11**. The following conditions are absolute contraindications:
    - Patients who developed severe toxicity to any specific ARV (hepatitis or Stevens - Johnson syndrome from NVP or EFV, severe anaemia from AZT, ABC hypersensitivity) must **NEVER AGAIN** be given a regimen containing the responsible ARV.
    - Do not use **TDF**-containing regimens in severe **renal failure** (creatinine clearance <50ml/min).

11.2.8 Adverse events / side effects

- Chose the appropriate alternative regimen from **Alternative 1** for patients with:
    - Contraindications
    - Significant side-effects (immediately)
    - Troubling side effects that did not improve within 2 weeks with symptomatic treatment.
- Use **Alt. 2** if **Alt. 1** can't be used due to previous toxicity or other specific contraindications.
- The appropriate 2nd line regimen depends on the 1st line regimen the patient was on when confirmed with treatment failure. Only certified **Level 2 ART providers** can initiate 2nd line.

11.2.9 Dosing and frequency

- **Table 12** shows the number of tablets to be taken by children and adults once or twice per day.
- 10 weight-bands are used to determine the number of paediatric tablets to be given.
- Most paediatric formulations are **tablets** that can be crushed if necessary. The only exceptions are:
    - LPV/r and ATV/r tablets must be **given whole** (not split or crushed).

- LPV/r for children **under 6kg** requires **liquid suspension** (80/20mg per ml) or **oral pellets** (40/10mg per capsule).

11.2.10 Use of DTG or EFV in women of reproductive age

- There is currently no confirmation that **DTG** is safe in very early pregnancy.[4] DTG-based regimens are therefore not used as standard 1st line regimens for girls and women who may get pregnant.
  - However, DTG may be given when consistent contraception can be assured, especially if other ARVs cannot be used.
- **EFV** is safe in pregnancy, including in the 1st trimester. Compared with NVP, EFV provides better long-term viral suppression, has fewer adverse events and less risk of resistance.[5]
  - Start **5A** as early as possible in pregnancy – including in the first trimester.
  - Don't change regimen if a woman got pregnant while on a EFV-containing ART regimen.

11.2.11 Use of Regimen 11 as *start regimen* for children under 3 years

- Children under 3 years often have a high viral load and may be infected with drug-resistant HIV from previous exposure to ARVs (mother's ART and/or infant nevirapine prophylaxis).
- Therefore, Children **under 3 years** respond better when **started immediately on a 2nd line** regimen (Regimen **11**).
- Starting children on Regimen **11** requires more differentiated follow-up and mothers need more hands-on support to ensure proper swallowing and adherence to dosing:
  - Regimen **11** has a higher pill burden than the standard *Start Regimen* for children (**2**).
  - Choose the right formulation: Children **under 6kg** need LPV/r **liquid** (needs fridge, has bad taste) or **oral pellets** (heat stable, taste masked). Move from LPV/r pellets to paediatric tablets as soon as the child is able to swallow whole tabs. LPV/r tablets must be swallowed whole and cannot be broken, crushed or dissolved.
  - Demonstrate how to give ARVs (see below how to give pellets) and CPT.
  - Observe regularly how the mother gives the meds. Ensure the full dose is properly swallowed.
  - Monitor **VL** at **6** and **12** months and every **12** months thereafter.
- Sites that can ensure the additional support (above) should routinely start all children under 3 years on Regimen **11**.
  - Don't delay ART initiation if regimen 11 is not immediately available / feasible. Start on regimen 2 instead and move to regimen 11 when possible.
- How to give **LPV/r oral pellets**:
  - Oral pellets are inside capsules. **Never give the actual capsule to swallow**.
  - Take out the required number of capsules and immediately close the bottle.

[4] http://www.who.int/medicines/publications/drugalerts/Statement_on_DTG_18May_2018final.pdf

[5] Use of efavirenz during pregnancy: a public health perspective. Technical update on treatment optimization. Geneva, World Health Organization, 2012 (www.who.int/hiv/pub/treatment2/efavirenz/en, accessed 2 December 2013).

- Hold the capsule on both ends and twist in opposite directions while pulling apart.
- Empty pellets onto a clean spoon / into a feeding cup with expressed breastmilk. Immediately give to the infant. For children over 6 months: mix with phala or age-appropriate food to mask the taste.
- Make sure the infant does not aspirate the pellets (coughing, choking, gagging).
- **Do not allow the pellets to dissolve / crush / stir the pellets** as this will release the unpleasant taste and reduce absorption.
- Throw away the empty capsule.

Table 11: Standard ART Regimens (all strengths in mg)

Regi-men	Paed. Formulation	Adult Formulation	Used for ART initiation 'Start regimen'	Line	Prescriber level	Starter pack	'Tail' needed	Contraindications	Possible adverse reaction	If confirmed, use Alt 1	If confirmed, use Alt 2
0	**ABC** 60 / **3TC** 30 + **NVP** 50	**ABC** 600 / **3TC** 300 + **NVP** 200	No	1st	1	Yes	Yes	• ABC hypersensitivity • Jaundice / hepatitis	• Fever, body pains, vomiting, cough [6] • Hepatitis, rash • Treatment failure	2 ABC/3TC+EFV 7	6, 5, NS 5, 4 8
2	**AZT** 60 / **3TC** 30 / **NVP** 50	**AZT** 300 / **3TC** 150 / **NVP** 200	• Standard for children and adults under 30kg	1st	1	Yes	Yes	• Anaemia <8g/dl • Jaundice / hepatitis	• Anaemia, vomiting, appetite loss • Hepatitis, rash • Lipodystrophy Lactic acidosis • Treatment failure	0 or 5 4 5 7	6 5 6, NS 9
4	**AZT** 60 / **3TC** 30 + **EFV** 200	**AZT** 300 / **3TC** 150 + **EFV** 600	No	1st	1	No	Yes	• Anaemia <8g/dl • History of psychosis	• Anaemia, vomiting, appetite loss • Lipodystrophy, lactic acidosis • Hepatitis, rash[7], psychosis, gynaecomastia[8] • Treatment failure	5, 0 5 2, 0 7	6 6 9
5		**TDF** 300 / **3TC** 300 / **EFV** 600	• Standard for girls and women 30kg+ who may get pregnant while on ART	1st	1	No	Yes	• History of psychosis • Uncontrolled BP↑/ diabetes, renal failure	• Renal failure • Hepatitis, rash[7], psychosis, gynaecomastia[8] • Persistent dizziness, visual disturbances • Treatment failure	0 [9,17] 6 6 8 [17]	2 [10,17] 0, 2 [17] 0, 2 [17] 9, NS [17]
6		**TDF** 300 / **3TC** 300 + **NVP** 200	No	1st	1	Yes	Yes	• Jaundice/Hepatitis • Uncontrolled BP↑/ diabetes, renal failure • Child under 3 years	• Renal failure • Hepatitis, rash • Treatment failure	0 [9,17] 5 8 [17]	2 [10,17] NS 9 [17], NS
7		**TDF** 300 / **3TC** 300 + **ATV/r** 300/100	No	2nd	2	No	No	• Uncontrolled BP↑/ diabetes, renal failure • Patient on rifampicin [11] • Pre-existing jaundice or suspected hepatitis [12]	• Renal failure • Jaundice [13] • Treatment failure [14]	8 [9,17] 10 12	NS

[6] Fever, body pains, vomiting, cough / sore throat and breathing problems can be due to life-threatening ABC hypersensitivity (rare). Stop all ARVs immediately. Never re-start ABC.

[7] Mild skin rash and/or dizziness and nightmares are common after starting EFV. This usually resolves by itself and is not usually a reason to interrupt or change regimen.

[8] EFV can cause breast enlargement in children and men (one side or both sides). This may resolve spontaneously while continuing EFV, but NVP substitution is usually needed (and effective).

[9] Patients with CrCl <50 ml/min need lower dose 3TC but full dose ABC. Combine ABC/3TC paed tabs and ABC (single) tabs for the correct dose ratio. Call the HIV Dept. logistics hotline for special order of ABC (single) tabs (see page **94**).

[10] AZT dose needs to be reduced from CrCl <15.

[11] Do not combine ATV/r with rifampicin (TB treatment). See **section 14** on page **67** for recommended ART regimen while on TB treatment.

[12] Do not start patients with pre-existing jaundice or suspected hepatitis on ATV/r. Use LPV/r instead.

[13] ATV/r can cause jaundice. Mostly, this is only of cosmetic concern. Refer jaundice to a specialist for LFT. If only indirect bilirubin is raised, continue ATV. Stop ATV/r if LFT cannot be done.

[14] Treatment failure on 2nd line ART and DTG-based regimens need confirmation of resistance mutations by genotyping before switch can be considered.

Regi-men	Paed. Formulation	Adult Formulation	Used for ART initiation 'Start regimen'	Line	Prescriber level	Starter pack	'Tail' needed	Contraindications	Possible adverse reaction	If confirmed, use Alt 1	Alt 2
8		**AZT** 300 / **3TC** 150 + **ATV/r** 300/100	No	2nd	2	No	No	• Anaemia <8g/dl • Patient on rifampicin [11] • Pre-existing jaundice or suspected hepatitis [12]	• Anaemia, vomiting, appetite loss	7	9
									• Lipodystrophy, Lactic acidosis	7	
									• Jaundice [13]	11	
									• Treatment failure [14]	12	
9	**ABC** 60 / **3TC** 30 + **LPV/r** 100/25	**ABC** 600 / **3TC** 300 + **LPV/r** 200/50	No	2nd	2	No	No	• ABC hypersensitivity	• Fever, body pains, vomiting, cough [6]	11	10
									• Diarrhoea, vomiting, dizziness, headache		
									• Treatment failure [14]	12	
10		**TDF** 300 / **3TC** 300 + **LPV/r** 200/50	No	2nd	2	No	No	• Uncontrolled BP↑/ diabetes, renal failure	• Renal failure	11 [9,17]	8 [9,17]
									• Diarrhoea, vomiting, dizziness, headache	7	8 [17]
									• Treatment failure [14]	12	
11	**AZT** 60 / **3TC** 30 + **LPV/r** 100/25	**AZT** 300 / **3TC** 150 + **LPV/r** 200/50	• Preferred start regimen for children under 3 years at sites with extra support (page **50**)	2nd	2	No	No	• Anaemia <8g/dl	• Anaemia, vomiting, appetite loss	10	7
									• Lipodystrophy, lactic acidosis	10	7
									• Diarrhoea, vomiting, dizziness, headache	8	7
									• Treatment failure [14]	12	
12		**DRV** 600 + **r** 100 + **DTG** 50 (± NRTIs)	No	3rd	2	No	No		• Diarrhoea, vomiting, headache, dizziness	NS	
									• Neuropathy	NS	
									• Rash, jaundice	NS	
13		**TDF** 300 / **3TC** 300 / **DTG** 50	• New standard for males 30kg+ and women 45 years+	1st	1	No	No	• Renal failure • Uncontrolled BP↑, uncontrolled diabetes • (Hepatitis B or C) [16]	• Renal failure	15	
									• Insomnia, headache, nausea, diarrhoea[15]	5	
									• Hepatitis [16]	5	6 [17]
									• Treatment failure [14]	(8)	(11)
14		**AZT** 300 / **3TC** 300 + **DTG** 50	No	1st	1	No	No	• Anaemia <8g/dl • (Hepatitis B or C) [16]	• Anaemia, vomiting, appetite loss	13	5
									• Insomnia, headache, nausea, diarrhoea [15]	4	
									• Hepatitis [16]	4	
									• Treatment failure [14]	(7)	(10)
15		**ABC** 600 / **3TC** 300 + **DTG** 50	No	1st	1	No	No	• ABC hypersensitivity • (Hepatitis B or C) [16]	• Fever, body pains, vomiting, cough [6]	13	5
									• Insomnia, headache, nausea, diarrhoea [15]	ABC/3TC + EFV	4, 0
									• Treatment failure [14]	(7)	(10)

[15] DTG is very well tolerated. Mild headache, insomnia, nausea and diarrhoea usually subside without regimen change.

[16] DTG may worsen liver damage in patients with viral Hepatitis (B or C). Check transaminases before and after starting DTG in patients with known Hep B or Hep C.

[17] Do Hep B test before taking patient off TDF-based regimen to avoid flare-up of undiagnosed Hep B. Add entecavir to ART regimen that does not contain TDF to control Hep B.

Table 12: Standard pack sizes and dosing of Paediatric and Adult formulations of ARVs, IPT and CPT

Drug	Tablets per tin		3 – 3.9 kg		4 – 5.9 kg		6 – 9.9 kg		10 – 13.9 kg		14 – 19.9kg		20 – 24.9kg		25 – 29.9kg		30 – 34.9 kg		35 – 39.9 kg		40 kg +	
	Paed.	Adult	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
NVP	60	60	1	1	1	1	1 ½	1 ½	2	2	2 ½	2 ½	3	3	1	1	1	1	1	1	1	1
AZT / 3TC	60	60	1	1	1	1	1 ½	1 ½	2	2	2 ½	2 ½	3	3	1	1	1	1	1	1	1	1
AZT / 3TC / NVP	60	60	1	1	1	1	1 ½	1 ½	2	2	2 ½	2 ½	3	3	1	1	1	1	1	1	1	1
ABC / 3TC	60	60	1	1	1	1	1 ½	1 ½	2	2	2 ½	2 ½	3	3	1	0	1	0	1	0	1	0
LPV / r liquid / tabs	60	120	*1ml*	*1ml*	*1.5ml*	*1.5ml*	2	1	2	1	2	2	2	2	3	3	3	3	2	2	2	2
LPV / r pellets (in caps)	120		2	2	2	2	3	3	4	4	5	5	6	6								
EFV	90	30							0	1	0	1 ½	0	1 ½	0	2	0	2	0	1	0	1
ATV / r		30															0	1	0	1	0	1
TDF / 3TC		30															0	1	0	1	0	1
TDF / 3TC / EFV		30																	0	1	0	1
TDF / 3TC / DTG		30															1	0	1	0	1	0
DTG		30															0	1	0	1	0	1
DRV		60																	1	1	1	1
r		60																	1	1	1	1
ETV		120																	2	2	2	2
RAL		60																	1	1	1	1
CTX 120	1000		0	1	0	1	1	1	1	1	2	2	2	2								
INH 100	100		0	½	0	½	0	1	0	1½	0	2	0	2½								
CTX 480		1000					0	½	0	½	0	1	0	1	0	2	0	2	0	2	0	2
CTX 960		1000									0	½	0	½	0	1	0	1	0	1	0	1
INH 300		672									0	½	0	½	0	1	0	1	0	1	0	1

11.3 Choosing regimen and time of starting in special situations

Table 13: Choosing ART regimen and timing of initiation in special situations

Condition	Timing for ART initiation	Less than 30kg	30kg +	
			Males / Women 45 years+	Girls / Women who may get pregnant
Anaemia (<8g/dl)	• As soon as possible	**0P / 0A**	**13A**	**5A**
Active TB	• Within 14 days of diagnosis • TBT + ART can be started on the same day if the patient is stable. Don't delay TBT or ART	See **Figure 4** on **page 69**		
Jaundice	• Refer to District or Central Hospital • After investigation and stabilisation	**4P / 4A**	**13A**[18]	**5A**
1st trimester pregnancy	• As soon as possible			**5A**
In labour (new HIV+)	• As soon as possible			**5A**
Renal failure	• Refer to District or Central Hospital • Start within 7 days of diagnosis	**0P / 0A**	**15A**	**0A**
Psychiatric Illness (history)	• As soon as possible • Reliable guardian needed	**2P / 2A**	**13A / 6A**	**6A**

11.4 Non-standard (NS) ART regimens

- Only expert ART clinicians can initiate NS regimens.
- Patients with multiple contraindications and/or adverse reactions against all standard NRTIs (TDF, AZT, ABC) or NNRTIs (NVP, EFV) may need a NS regimen.
- Consider ATV/r or LPV/r for substitution of DTG, NVP and EFV.
- Contact the DHA for availability of non-standard ARVs (see **section 24** on **page 107**).
    - Provide patient history, indication and proposed regimen.

[18] Regimen 13A can only be used if severe liver damage (ascites; albumin <2.8g/dL; total bilirubin >50mmol/L; encephalopathy) and/or viral hepatitis B or C have been ruled out.

12 Prescribing and dispensing ARVs

Key Facts: Prescribing and dispensing ARVs

- ARVs should be taken after the same number of hours every day (e.g. every 12 or every 24 hours). Most ART regimens can be taken in the morning, at noon or at night and it does not matter if they are taken before, after or with food.
    - DTG (regimen 13A and 14A) can disturb sleep and should therefore be taken in the morning.
    - EFV (regimen 4 and 5) can cause dizziness, especially in the first 4 weeks. This is less troublesome when taken before bed.
- **Missing a dose**: what to do if a patient remembers to take his ARVs late? If the patient remembers:
    - **Less than half-way** to the next scheduled dose: take the missed dose immediately, and take the regular next dose at the normal time.
    - **More than half way** to the next scheduled dose: skip the missed dose and take the regular next dose at the normal time.
- Dispense ARVs only in the original sealed container. Only exception: open containers to dispense the precise number of tablets needed for *Starter Packs.* [1]
- Only the patient or his registered guardians/treatment supporter is allowed to collect ARVs.
- In an emergency, patients are allowed to collect ARVs from any ART clinic in Malawi following special rules (see below).

12.1 Rules for prescribing and dispensing of ARVs

ARVs for treatment of HIV (ART)

- Only MOH-certified clinical ART providers are authorized to **prescribe** ART: Medical Doctors; Clinical officers; Medical Assistants; Registered Nurses; Nurse/Midwife Technicians.
- Only health workers and qualified pharmacy personnel are allowed to **dispense** ARVs.
- ARVs may be dispensed at MOH-certified static ART clinics and in outreach locations. Outreach clinics must be staffed by certified ART providers. ARVs may not be distributed outside of these settings.
- Only the patient or his individual registered guardian/treatment supporter are allowed to **collect** ARVs.

ARVs for PEP

- PEP needs to be started as soon as possible after high risk exposure. Such events are often managed under challenging circumstances (e.g. rape, accidents).

- Non-health professionals (e.g. police officers) are allowed to dispense the initial dose of PEP without prior confirmation of HIV negative status under the following circumstances:
    - Received PEP training by a MOH certified ART provider.
    - Under regular supervision by ART clinic staff
    - DHOs are responsible for supplying and accounting for ARVs given to e.g. *Victim Support Units* and must provide active support with ARV stock management.

Emergency dispensing to patients from another PMTCT/ART site

- In an emergency, patients are allowed to collect ARVs from any ART clinic in Malawi under the following conditions:
    - The patient must present an ART identity card or the health passport with ARV dispensing information.
    - If in doubt about a patient's authenticity, confirm by calling the site where the patient is registered.
    - Document emergency ARV dispensing in the patient's health passport.
    - ARV dispensed to patients registered at another site must be recorded in the *Emergency ARV Dispensing Register.* Improvise a hardcover register: Date, original ARV registration number, original facility name, patient name and contact details, ARV name and quantity dispensed, reason for emergency dispensation, staff name.
    - Instruct patient to return to their ART clinic of registration as soon as possible to ensure the patient is not recorded as defaulter.

12.2 Determining quantities to be dispensed and next appointment

- **Table 14** on page 59 shows the number of tablets to be supplied for appointment intervals of 2, 4, 8 or 12 weeks for the total number of tablets taken of each ARV per day (paediatric and adult formulations).
    - Use **Table 12** to add up the 'total tablets taken per day' for each ARV contained in the regimen. For example: a child of 15kg on AZT/3TC/NVP (Regimen 2) takes **2½** paediatric tablets in the morning and **2½** tablets in the evening, adding up to **5** total tablets per day.
    - The *Actual number of tablets needed* is the minimum number of total tablets the patient needs to take home to cover the time to the next appointment. (Total tablets = tablets remaining from the previous visit **+** tablets newly dispensed). The number needed includes an extra 2-day supply to act as a safety-buffer. The total tablets must meet or exceed the *Actual number of tablets needed*.
    - Different ARVs come in tins of 30, 60, 90 or 120 tablets (see **Table 12**). Given that only full tins should be dispensed, the number of tablets needed is *rounded up* to multiples of full tins.
    - *Rounding up* may result in a considerable *over-supply*. For some regimens and dosages, perfectly adherent patients will be left with more than half a tin of ARVs at their next appointment. Explain this to the patient / guardian and emphasize the importance of keeping the next appointment.

- The number of tablets expected to be used in the interval is shown for 'perfect adherence' (100%) and for 'good adherence' (95%-105%).
- Calculate the number of tablets used by subtracting total tablets remaining at the current visit from total tablets available at the end of the previous visit.

12.3 Appointment / dispensing interval

- Give next appointment date at least 2 days before ARVs would be finished to allow for the safety buffer.
- Take account of the weekly ART clinic schedule (e.g. Mondays + Wednesdays) when giving the next appointment. Appointments are usually given for 2 weeks (starter pack), 4, 8 or 12 weeks.
- Patients initiating standard or alternative first line ART have to be reviewed clinically after **2 weeks** if they have been given a starter pack / otherwise after **1 month** and then **every month for the first 6 months**.
- Thereafter, stable and adherent patients can be given up to 12-week (**3-month**) appointments.
- In exceptional cases (e.g. international travel), up to **6** or even **12 months** of ARVs can be dispensed.
- Patients starting 2nd line ART have to be seen every 4 weeks for the first 6 months. Thereafter, patients who are stable and adherent to 2nd line ART can be given up to 8-week appointments.
- Align dispensing of CPT and IPT with ART visits.
- Push back appointment date to allow patients to use up accumulated 'hanging' tablets, e.g. give an appointment after 5 instead of 4 weeks.

Table 14: Quantity of ARVs to be supplied by visit interval and daily dose

Note: *supply and consumption must be calculated separately for each component in the regimen.*
Example: separate calculation for AZT/3TC and AZT/3TC/NVP making up a starter pack of Regimen 2

Dispens. interval	Total tabs taken per day	Supply needed								Total tabs **USED** in interval - Adherence	
		Actual	*Multiples of full tins*								
			Tins of 30		Tins of 60		Tins of 90		Tins of 120		
		tabs *	tabs	**tins**	tabs	**tins**	tabs	**tins**	tabs	**tins**	**Perfect** 100%	**Good** 95% – 105%
2 weeks	1	***16***	30	**1**	60	**1**	90	**1**			14	*14 – 14*
	1 ½	***24***			60	**1**	90	**1**			21	*20 – 22*
	2	***32***			60	**1**	90	**1**			28	*27 – 29*
	2 ½	***40***			60	**1**					35	*34 – 36*
	3	***48***			60	**1**					42	*40 – 44*
	4	***64***			120	**2**					56	*54 – 58*
	5	***80***			120	**2**					70	*67 – 73*
	6	***96***			120	**2**					84	*80 – 88*
4 weeks	1	***30***	30	**1**	60	**1**	90	**1**			28	*27 – 29*
	1 ½	***45***					90	**1**			42	*40 – 44*
	2	***60***			60	**1**	90	**1**			56	*54 – 58*
	3	***90***			120	**2**			120	**1**	84	*80 – 88*
	4	***120***			120	**2**			120	**1**	112	*107 – 117*
	5	***150***			180	**3**					140	*133 – 147*
	6	***180***			180	**3**			240	**2**	168	*160 – 176*
	8	***240***			240	**4**					224	*213 – 235*
	9	***270***			300	**5**					252	*240 – 264*
8 weeks	1	***58***	60	**2**	60	**1**	90	**1**			56	*54 – 58*
	1 ½	***87***					90	**1**			84	*80 – 88*
	2	***116***			120	**2**	180	**2**			112	*107 – 117*
	3	***174***			180	**3**			240	**2**	168	*160 – 176*
	4	***232***			240	**4**			240	**2**	224	*213 – 235*
	5	***290***			300	**5**					280	*266 – 294*
	6	***348***			360	**6**			360	**3**	336	*320 – 352*
	8	***464***			480	**8**					448	*426 – 470*
	9	***522***			540	**9**					504	*479 – 529*
12 weeks	1	***86***	90	**3**	120	**2**	90	**1**			84	*80 – 88*
	1 ½	***129***					180	**2**			126	*120 – 132*
	2	***172***			180	**3**	180	**2**			168	*160 – 176*
	3	***258***			300	**5**					252	*240 – 264*
	4	***344***			360	**6**					336	*320 – 352*
	5	***430***			480	**8**					420	*399 – 441*
	6	***516***			540	**9**					504	*479 – 529*

** Actual tabs needed includes a 2-day safety-buffer*

13 Starting ART

Key Facts: Starting ART

- ART does not cure HIV infection.
- ART stops the virus from multiplying, which allows the immune system to recover.
- The virus will 'wake up' as soon as ART is interrupted and it will learn how to evade ART. This means that ART may no longer work for this patient.
- Once started, ART must be taken every day for life. All patients need effective support:
    - Identify a reliable guardian / treatment supporter who needs to attend ART education.
    - Link with patient / peer support group
- Successful ART leads to very low levels of virus in blood, semen and vaginal fluids. This greatly reduces the risk of sexual or mother-to-child transmission. However, condom use is important
    - In the first 6 months after starting ART
    - Later if adherence is not good and/or viral suppression has not been confirmed.
- All patients need a confirmatory HIV test before starting ART (see **section 13.3** on **page 61**) to rule out any possibility of mix-up of test results or fraudulent access to ART.
- ARVs must not be dispensed outside of certified PMTCT/ART facilities (static or outreach) and must not be shared, sold or passed on to others.
    - Bring back any remaining ARVs at every clinic visit to allow the provider to count them.
    - Return unused ARVs (e.g. after a patient's death) to the clinic for proper disposal.
- Patients who are late for their ART appointment will be actively followed from the clinic (home visit, phone, guardian).
    - Ask for consent for active follow-up at the time of starting ART.
    - Patients can withdraw consent at any time.
- A small number of patients on ART develop serious side-effects. Educate all patients about the important signs to look out for (see *Key facts* on **page 65**)

13.1 When to start ART

Key Facts: Starting ART

- Start ART as soon as possible:
    - For all children and adults with **confirmed HIV infection**
    - For infants with **presumed AIDS** (following definition of PSHD).
- **All** patients need a confirmatory HIV test before starting ART.
- Explain the benefits of immediate ART for the patient's **own health**, and for **prevention** of onward transmission to sexual partners and from mother to child. This understanding is key for patient motivation and good adherence.
- Patients may not be ready to start ART immediately.
    - Allow for reflection time if the patient is unsure and/or wants to discuss with family.
    - Schedule a follow-up appointment not further than 2 weeks.

13.2 Record keeping

- PMTCT/ART nurse or clinician: fill ART patient cards immediately when ART eligibility is established (do not delegate this to HSA). For this reason, keep blank ART treatment cards at OPD, ANC, maternity, wards, etc.
- Dispensing of ARVs must be recorded on the patient treatment cards.
- Complete ART treatment cards before giving out the first supply of ARVs.
- Patients should only be entered in the ART register when receiving their first supply of ARVs.

13.3 Confirming HIV infection

- All patients need a confirmatory HIV antibody test to rule out a mix-up of test results or fraudulent access to ART:
    - Before starting ART
    - Patients who received confirmatory testing at pre-ART (before 2016) do not need another confirmatory test when starting ART.
    - All children under 24 months who start ART need a confirmatory DNA-PCR using a new DBS sample. This should be collected on the day of starting ART.
- Do not delay ART initiation if HIV test kits are not available for the confirmatory test, but do confirmatory test at the next scheduled visit as soon as testing is available.

13.3.1 Confirmatory testing for adults and children 2 years and above

- Place a dedicated HIV testing provider to the ART clinic to do confirmatory testing. Ensure that all Quality Assurance protocols for HIV testing (proficiency testing, quality control) are being followed.
- **Use the first and second rapid test in parallel** (currently Determine + Uni-Gold) for confirmatory HIV testing. Review **Figure 2** on **page 63** for the correct algorithm and interpretation of results:
- Test 1 and Test 2 are **both positive**:
    - Record ***'Confirmatory Positive'*** result in the **MOH HIV Rapid Testing register** (Version 3, January 2013)
    - Record confirmatory HIV test results on ART patient card.
    - Start ART
- Test 1 and Test2 are **discordant**:
    - Review testing protocol, quality control, expiry date and condition of test kits. Do immediate (parallel) repeat. Use a different (experienced) HIV testing provider if possible.
        - Both positive: see above
        - Discordant or both negative: see below
- Test 1 and Test2 are **both negative**:
    - Record ***'Confirmatory Inconclusive'*** in HIV Testing Register.
    - Collect DBS blood sample and send to reference lab and/or send patient to referral hospital to repeat regular HIV testing and for review by an experienced ART clinician.
    - Give follow-up appointment to review lab test result.

13.3.2 Confirmatory HIV testing for children under 2 years

- All children to be started on ART under the age of 2 years need a confirmatory DNA-PCR.
- Collect the DBS sample on / before the day of initiation.
- Don't delay ART initiation - don't wait for the confirmatory PCR result before starting ART.
- Review **Figure 3** on **page 64** for the schedule of follow-up testing and the correct action based on the results.

Figure 2: Confirmatory HIV testing for adults and children aged 2 years and above

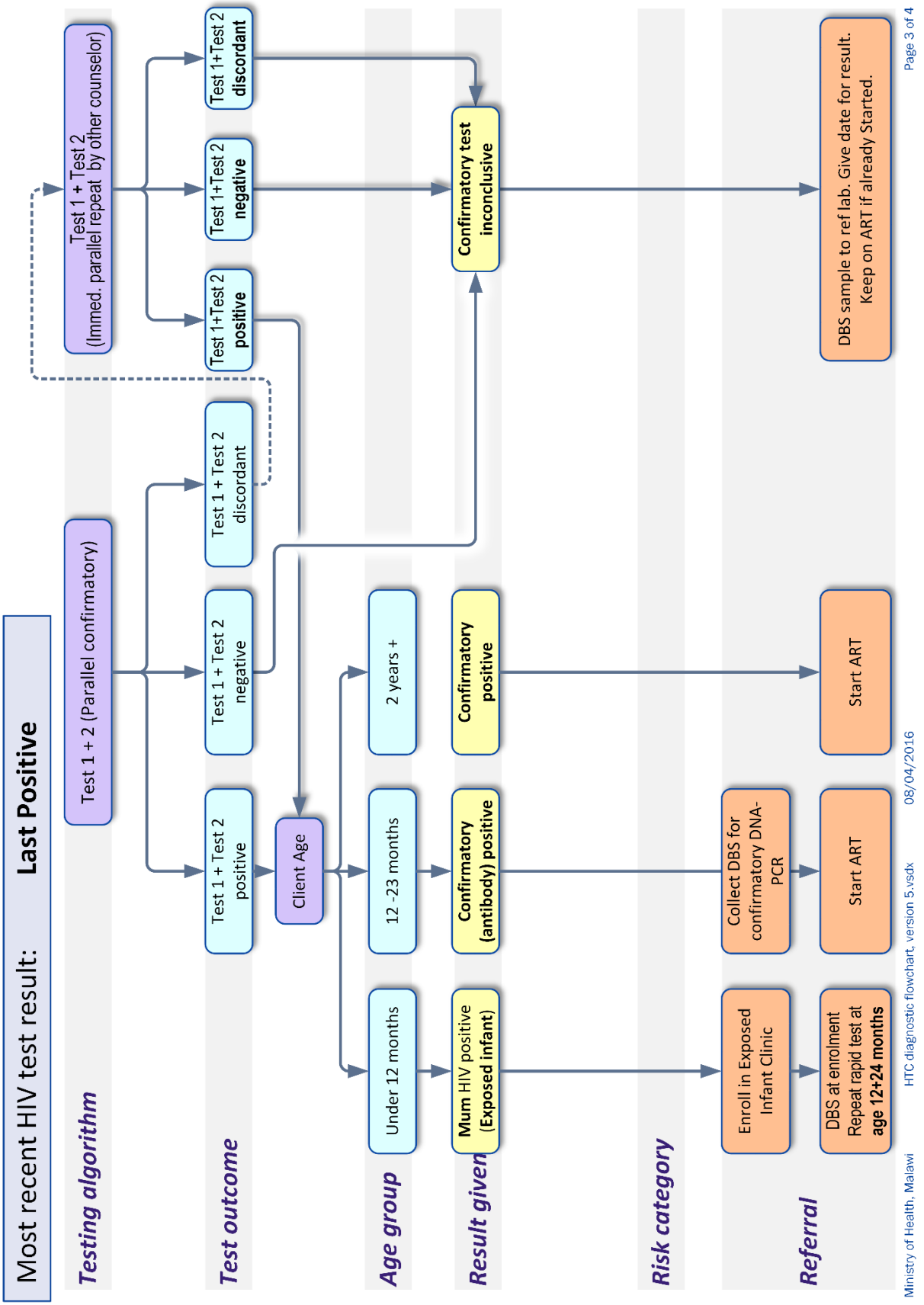
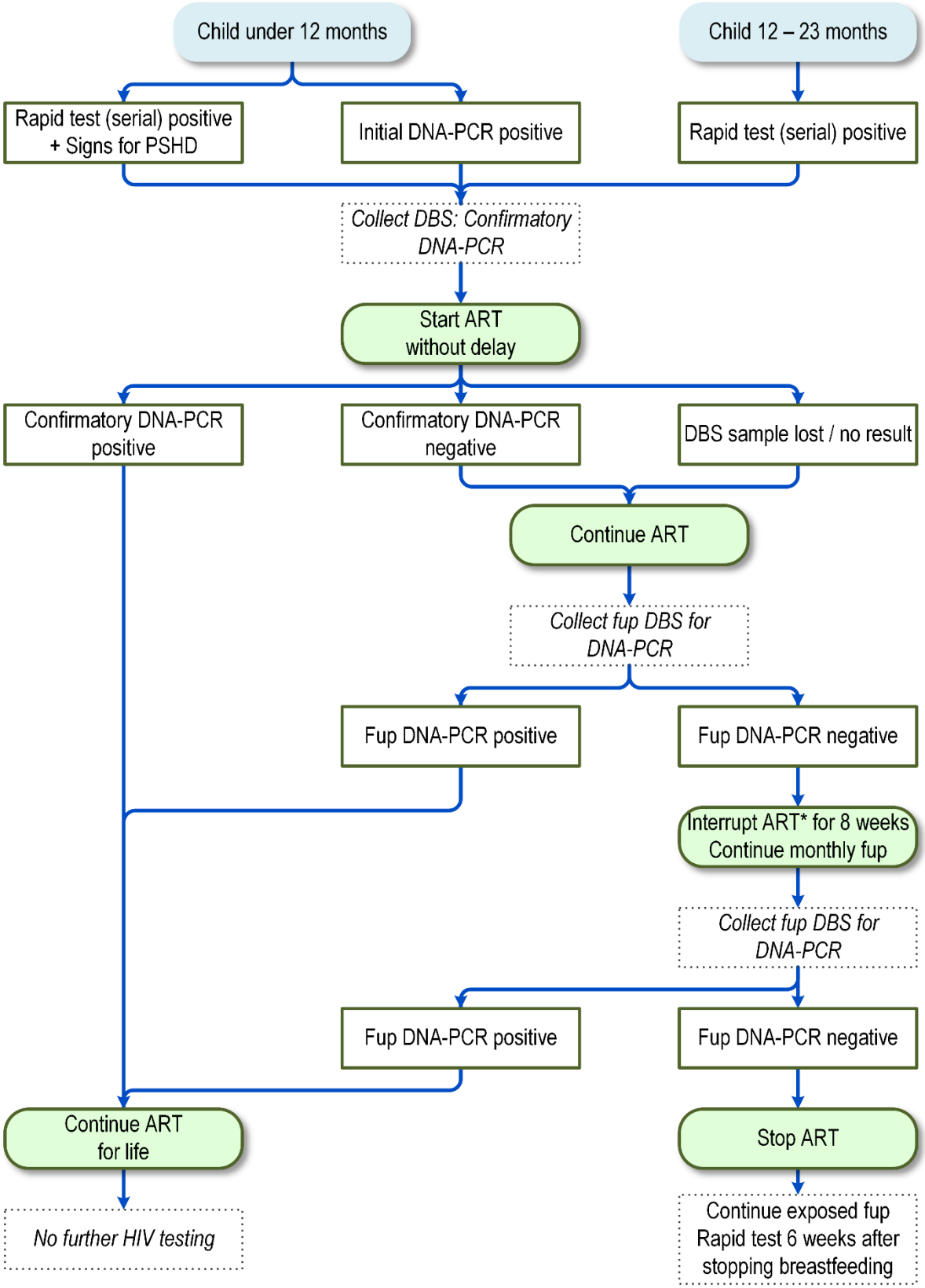


Figure 3: Confirmatory HIV testing for children under 2 years



* Give NRTI 'tail' when interrupting ART regimen 0P or 2P (see **section 11.2.6**on **page 49**).

13.4 Preparing the patient for ART

- Start ART as soon as possible after testing positive.
- Offer pregnant women to start ART on the same day of diagnosis.
- Confirm that patient (or parent/guardian if patient is <15 years) understands implications of ART and is committed to lifelong adherence.
- Identify long-term treatment support for patients who are unable to take responsibility for their own treatment (persons with mental disability or drug-addiction, etc.).
- Ask all patients to attend the initial group counselling and/or the ART initiation visit with a named guardian/treatment supporter.
    - Another patient can be appointed as the *named treatment supporter* if the patient is unable to identify a suitable guardian.

13.4.1 Mandatory patient education when starting ART

Key Facts: ARV side effects

- A small number of patients on ART develop significant side-effects.
- Most side-effects are mild and disappear while ART is continued.
    - DTG can **disturb sleep**, but this is rare when taken in the morning and usually settles by itself.
    - EFV can cause **bad dreams** and **dizziness** in the first few weeks of treatment, but this usually disappears by itself and it is important to continue treatment.
- Some side-effects require a regimen change.
    - Ask all men/boys on an EFV-containing regimen to monitor themselves for **swelling of the breast** (gynaecomastia). Report this at the next scheduled visit. Substitute EFV with DTG or NVP as soon as possible after onset to improve likelihood of full reversal.
- Very few patients develop serious side effects. Stop all drugs immediately and present to the hospital if any of the following conditions are seen:
    - **Yellow eyes** / **hepatitis**
    - Severe **stomach pain** and **vomiting**
    - Severe **skin rash** with blisters, involving eyes, mouth or genitals

- All patients must receive individual counselling at ART initiation.
- Women starting ART in labour can receive individual ART counselling after delivery.
- In addition, all patients should attend an ART group counselling session. Recommended practice:
    - Attended group counselling between 1 to 5 days before the day of ART initiation.
    - But: group counselling can be on the same day as initiation to avoid delay beyond 7 days.

- Pregnant women may attend the group counselling at the next scheduled visit to ensure they can start ART on the same day.
- Ask patients to attend with their named guardian (also see **section 13.3** on **page 61**).

ART group counselling

- Use the latest version of the MOH ART flip chart.
- Share "Key facts for providers and patients"
- Explain the standard VL monitoring schedule (see **page 78**). Ask the patients to help remember when VL is due.

Individual ART counselling

- Confirm that patient and guardian have understood the following:
  - Commitment to lifelong adherence
  - Dosage and interval of taking ARVs
  - Potential side-effects
  - Date of next appointment

13.5 Detecting and treating high blood pressure

Key Facts: BP screening

- 1 out of 3 adults in Malawi have hypertension and over 90% of these have not been diagnosed.
- Even without hypertension, HIV patients have a higher risk of stroke.
- Treating all hypertensive ART patients can prevent many cases of stroke, heart and kidney failure and other complications.
- Screen all adults (**30 years +**) for hypertension:
  - At least once at the time of ART initiation. Record BP on patient card header.
  - Aim to repeat BP screening at least every 12 months

13.5.1 Correct BP measurement method

- Make sure the patient is relaxed (rest at least 5 minutes after physical activity).
- Sit upright, remove clothing from upper arm that may restrict blood flow or interfere with BP cuff.
- Make sure BP cuff is the right size: check the arm circumference is within range shown on the cuff.
- If the initial reading is higher than **140** systolic and/or **90** diastolic:
  - Repeat reading twice. Wait for at least 5 minutes between readings.
  - Calculate the average between the 3 readings (separately for the systolic and diastolic values).

Classification	Systolic		Diastolic	Management
Mild	140-159	*and/or*	90-99	Try *lifestyle measures* alone, start stepped treatment if no normalization
Moderate	160-179	*and/or*	100-109	*Lifestyle measures* + stepped treatment
Severe	>180	*and/or*	>110	Urgent treatment *Lifestyle measures* + stepped treatment

13.5.2 Management of hypertension

- Start management for hypertension if the average of the 3 readings is higher than **140** systolic and/or **90** diastolic**.**
- Urgent treatment for severe hypertension if repeat reading is **180** systolic and/or **110** diastolic.
- Fill NCD patient card for monitoring and documentation.
- Screen for diabetes
- *Lifestyle measures*: Eat more veg and fruit, less meat / fat, reduce salt, stop smoking, exercise regularly, normalize weight, limit alcohol
- See ***Malawi Standard Treatment Guidelines 2015*** for stepped anti-hypertension treatment.

13.6 Baseline and routine lab investigations

- Do routine urine LAM and serum CrAg for patients with advanced HIV infection (see **section 8.1** on **page 22**).
- The national program does not require:
    - Routine baseline lab investigations before starting ART or routine investigations for ART toxicity.
    - Routine scheduled CD4 monitoring of patients on ART is not supported.
- Use targeted investigations if clinically indicated.
- Scheduled VL monitoring has been rolled out (see **section 15.10** on page **78**).

14 Combining ART and TB treatment

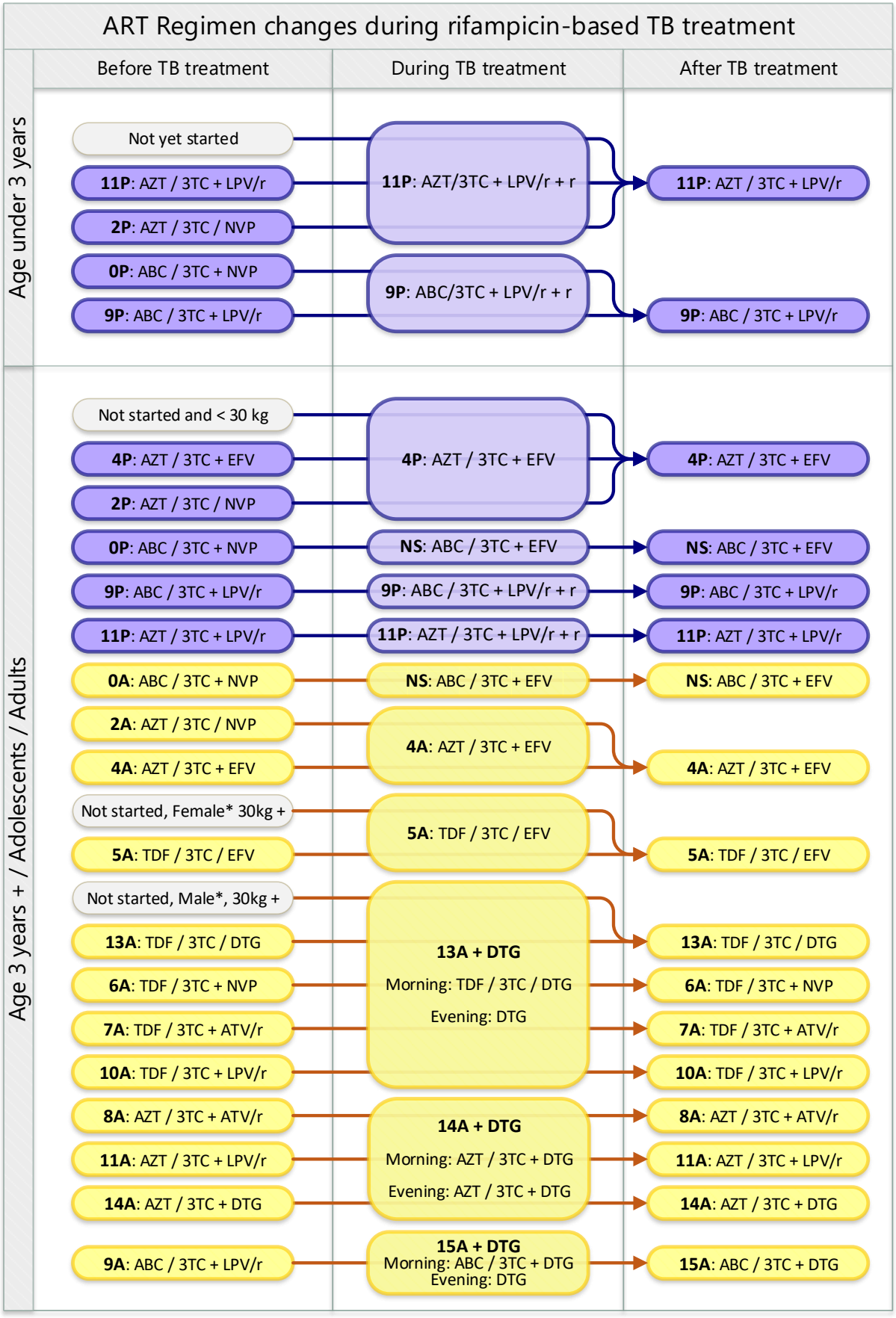
Key Facts: ART and TB treatment

- Each year, 15,000 (1%) of the 1.1 million HIV infected Malawians develop active TB and 6,000 die from TB[19].
- The risk of active TB is high for the first 6 months on ART and remains elevated for life.
- Most HIV patients with TB do not have typical TB symptoms (productive cough). Many are sputum smear negative.
- HIV infected TB patients must start ART and TB treatment as soon as possible. The long term outcome is poor if only one treatment is taken.

- NVP, ATV/r, LPV/r and DRV have significant interactions with rifampicin. Do not combine if possible.
- Use **Figure 4** to select the right ART regimen to give during rifampicin-based TB treatment. Use alternative regimens for patients with specific contraindications.
- DTG-based ART regimens (**13A, 14A, 15A**) are a good combination with TB 1st line treatment.
    - However, the daily dose of DTG needs to be doubled while on rifampicin-containing TB treatment: take the regular DTG-containing regimen in the morning and one additional tablet of DTG 50mg in the evening (after 12 hours).
    - Continue with double-dose DTG for 7 days after the last dose of rifampicin.
- DTG-based regimens are not used as standard 1st line for girls and women who may get pregnant while on ART (see **section 11.2.10** on **page 50**).
    - However, DTG-based regimens are the best option for patients previously on 6A, 7A, 10A and 11A who need TB treatment.
    - The benefits also outweigh potential risks for women of reproductive age. Ensure reliable contraception while on DTG and revert to previous regimen after stopping TB treatment.
- Patients with ART failure (see **section 6.9.9** on **page 60**) may develop active TB. In this case, 2nd line ART needs to be combined with TB treatment.
    - **Preferred:** Use **13A, 14A** or **15A** (with double dose DTG) while on TB treatment. Move back to previous ART regimen after TB treatment is completed.
    - **Alternative:** Use LPV/r-based 2nd line regimens (**9A**, **10A**, **11A**) for patients who cannot use **13A, 14A or 15A**.
        - Double the daily dose of LPV/r (4 tablets of LPV 200mg / r 50mg every 12 hours) for the duration of rifampicin treatment.
        - Patients previously on ATV/r-based regimens (**7A**, **8A**) move back to ATV/r once TB treatment has been completed.
    - Alternatively, replace rifampicin with rifabutin in patients on LPV/r (normal dose). Give rifabutin 150mg daily. Other TB drugs in the regimen should also be continued.

[19] 2016 Global tuberculosis report (WHO)

Figure 4: ART regimen changes during TB treatment for children and adults



- **Table 15** shows relevant interactions.
  - **Green:** Combination causes no problems
  - **Yellow:** Combination causes usually no problems but monitor patient for possibly increased side-effects or adjust dosage as shown
  - **Red:** Do not combine without specialist advice

Table 15: Relevant interactions between ARVs and TB drugs

	Isoniazid	Rifampicin	Rifapentine	Streptomycin	Ethambutol	Pyrazinamide
TDF	OK	OK	OK	renal toxicity	OK	OK
AZT	OK	OK	OK	OK	OK	OK
3TC	OK	OK	OK	OK	OK	OK
DTG	OK	OK double DTG dose	poss. hypersensitivity (don't combine)	OK	OK	OK
EFV	OK	OK	no experience needs EFV ↑	skin rash	OK	hepatitis
NVP	skin rash	start NVP full dose, hepatitis	no experience needs NVP↑	skin rash	OK	hepatitis
ABC	OK	OK	OK	OK	OK	OK
ATV/r	OK	no experience (don't combine)	no experience (don't combine)	OK	OK	OK
LPV/r	OK	major dose adjustment	no experience (don't combine)	OK	OK	OK

15 Continuing ART

15.1 Confirming adherence to appointment

- On the patient card, look at the *Next Appointment Date* given at the previous visit to confirm that the patient is not late.
- The patient is likely to have missed doses if s/he is more than 2 days late. Compare and validate with *Pill Count* and the reported number of *Doses Missed.*

15.2 Monitoring height and weight

- Record current weight (and height for children under 18 years).
- Look for weight changes compared with previous measurements. Patients are expected to normalize their weight in the first 6-12 months on ART.
- Classify nutrition status for children based on *CMAM* guidelines.
- Investigate any consistent weight loss over 2 or more consecutive visits. Remember to confirm that the scale is correctly calibrated and any heavy clothing was removed.

15.3 Monitoring for HIV-related diseases and drug side-effects

- Use the standard clinical monitoring checklist for HIV patients to actively screen for symptoms of HIV-related diseases and/or drug side effects.
- Use the syndromic guide shown in **Table 16** on **page 82** to identify the likely cause of symptoms and to choose the right primary and secondary management.
- A symptom that could be caused by an HIV-related disease or by a side-effect is more likely a side-effect if it started or worsened after the start of medication.
- Circle side-effects Yes / No on the patient card and specify new side effects under *Notes*.
- Change the ART regimen if medically indicated (see below).
- Write any new HIV-related disease under *Notes* on the back of the patient card.

15.4 Indications for interrupting or stopping ART

- Stop ART in patients with chronic poor adherence. Consider stopping if intensive counselling has failed.
- ART should be stopped abruptly and completely if any of the following severe side-effects are suspected:
    - Lactic acidosis
    - Pancreatitis
    - Severe hepatitis
    - Stevens-Johnson syndrome

- Stopping ART in patients with less severe toxicity against EFV or NVP (skin rash, psychiatric effects) should be done by giving a 'tail' of the other 2 ARVs for 7 days to prevent 'monotherapy' due to the long half-life of NVP and EFV (see **Table 11** on **page 52**).

15.5 Selecting regimen and formulation for continuation

- Don't change regimen without clear medical indication. Unnecessary changes spoil future treatment options.

Do NOT change ART regimen:

- If a patient has moderate dizziness / drowsiness / nightmares in the first 2-4 weeks of starting a regimen with EFV (regimen 4 or 5. Also see footnote on **page 52**).

Change dosage and formulation:

- Review current weight for children and adjust dosing if necessary. Children on 1st line regimens change to adult formulation and dosage when their weight is over 25kg (see **Table 12** on **page 52**).
- Start a new *ART Patient Card – Adult ARV Formulations* for children who change from paediatric to adult ARV formulation. File together with the old card.

Change ART regimen:

- Use **Table 11** on **page 52** to select the appropriate alternative regimen. Change patients with significant side-effects immediately. Change patients with troubling side-effects that did not improve after 2 months of symptomatic treatment.
- Children who were on paediatric 2nd line regimen (Regimen 9P) routinely change to standard adult 2nd line regimen (Regimen 7A) once they **weigh over 30kg**. This is to reduce the pill burden while continuing on an equally effective regimen.
- **Routinely change** adolescent boys who were on **2A** to **13A** once they **weigh over 30kg**.
- Add any new regimen to the *ART Regimens* history section on the card header and specify any non-standard regimen here.
- Multiple contraindications / side-effects may require NS regimen (see Section **11.4** on **page 55**)

15.6 Routine TB screening (*intensified case finding*)

- Screen all patients at each visit for signs of active TB using 4 standard screening questions
    - Cough of any duration
    - Fever
    - Night sweats
    - Weight loss / failure to thrive / malnutrition

- Classify screening outcome as follows:
    - ***TB not suspected*** if none of the 4 signs are positive. In this case, the patient is very unlikely to have active TB.
    - ***TB suspected*** if one or several of the 4 signs are positive.
        - Thoroughly investigate further (full clinical exam, sputum for Xpert, chest x-ray, fine needle aspirate, etc.).
        - Interrupt IPT until active TB has been ruled out
    - ***TB confirmed*** if the patient has a current confirmed episode of TB (clinical or lab diagnosis).
        - Always confirm if the patient is currently taking and adherent to TB treatment – initiate TB treatment without delay or provide intensive adherence support.
        - Classify ***on TB treatment*** or ***not on treatment.***

15.7 Achieving optimal adherence

Key Facts: ARV adherence

- Patients must take more than 95% of doses at the prescribed interval for life to prevent HIV drug-resistance. Repeated skipping of individual doses or repeated longer interruptions inevitably lead to development of HIV drug-resistance.
- **Example:** HIV drug-resistance will develop if a patient on Regimen 5A (TDF/3TC/EFV) continues to skip more than **3 tablets** in every **8-week** period.
- Children and adolescents on ART need special support (see **page 75**).

15.7.1 Routine adherence support

- Ask at every clinical assessment visit:
    - What challenges have you had taking your ARVs?
    - What days / time of day are you most likely to forget taking your meds? (Weekends, weekdays, mornings, evenings?)
- Remind patients of the importance of perfect adherence at every clinic visit:
    - Initial ART counselling
    - Follow-up group counselling
    - Start *intensive adherence counselling* (**IAC**) if any sign for poor adherence (see **page 74**)
- Give **practical strategies** how to achieve optimal adherence:
    - Build ARVs into the daily routine (e.g. before washing the face, after evening meal)
    - Ask family or friends to remind
    - Set a daily alarm on the cell phone

- Keep a 'drug diary' and mark every tablet taken

- Encourage honest dialogue. Avoid giving the impression of 'policing' the patient. Work with patients to help them achieve good adherence.
- Poor adherence always has valid reasons and most can be resolved: vomiting, transport problems, domestic problems, (perceived) side effects, psychological problems, wrong understanding, etc.

15.7.2 Intensive adherence counselling

Indications

- Questionable or confirmed poor adherence noted at regular visit / late for appointment
- Routine VL result **above detection limit**, even if the results is <1000 copies/ml (suspected treatment failure).

Step-by-step guide

- Ask both patient and the treatment supporter to attend.
- Explain the information presented in the boxes with **Key facts**:
  - Starting ART (page **60**)
  - Achieving optimal adherence (page **73**)
  - Monitoring for treatment failure / HIV drug resistance (page **77**)
- Make a (verbal) ***contract*** with the patient and the treatment supporter:
  - "We will check your VL again in 3 months."
  - "We will work together to help you remember to take your tablets as prescribed. This will help us find out if your current ARVs are still able to make your ***VL undetectable***."
- Identify the specific problems / situations that get in the way of good adherence. Ask for:
  - Frequent travel / boarding school
  - Conflicts at home / lack of privacy / stigma
  - Alcohol / drug problems
  - Mood disorder / depression
- Agree on an action plan and write instructions in health passport: select the most suitable **practical strategies** from **page 73**. Review specific strategies for children / adolescents (**page 75**)
- Consider giving monthly appointments until follow-up VL is due (after 3 months of good adherence).
  - Do pill count and assess adherence closely at each follow-up visit
  - Review action plan: what has worked – what has not? Revise plan if necessary.

15.8 Special treatment support for children and adolescents

Key Facts: Adherence support for children / adol.

- Good adherence is particularly challenging for children and adolescents:
  - Dependence on caregivers, often in difficult home environment.
  - Need to adjust ARV dose by body weight.
  - Developmental and psychosocial changes.

- Ask at every visit:
  - Who is responsible for supervising the taking of ARVs?
  - Who stands in for the guardian if s/he is away?
  - How do you give the tablets?
- Discuss selecting a trusted teacher or fellow student as treatment supporter for children attending boarding school.
  - Offer to transfer the child to the most convenient ART site closest to school.
- Children (just like any other patients) who are adherent and stable on ART can be given 3 months of drug supply or more if necessary.

15.8.1 Managing the disclosure process

- Explain to the parent that disclosure is a gradual process. Assure the parent that you will work through this process together.
- Remind parents / care givers at every clinic visit that it is very important to talk to the child about their HIV infection and ART status.
- Don't isolate the child behind a "wall of secrecy and silence". Remember the child probably knows more than you think.
- Never lie or make up stories about the child's HIV infection and the drugs they are taking (e.g. misrepresenting ARVs as TB drugs or vitamins). Lies will eventually come out and undermine trust and make the child feel guilt, shame and will damage self-esteem and may lead to poor adherence.
- Ask parents at every visit how far they have come in the disclosure process.
- Encourage parents to talk directly to their child in the environment they feel most comfortable. Offer to take part in the discussion if parents are uncomfortable doing this on their own.

From age 5-7 years:

- Explain that the child has a germ that requires taking drugs every day to keep the germ 'asleep'.
- Full disclosure can begin as early as 8-10 years.

By age 11-13 years:

- Add more information gradually. By age 11-13 years the child should know that s/he has HIV. Also, all of the following should have been explained:
    - Touching, cuddling and kissing are safe.
    - Sharing soap, towel, plates and cutlery is safe.
    - Don't share needles or razor blades. HIV and other diseases can travel in traces of blood and infect the other person.

From puberty / adolescence:

- Invite open dialogue about 'teenage challenges' that can get in the way of good adherence:
    - Low self-esteem, pill fatigue, frustration about the need for ART
    - Conflicts at home / at school
    - Relationships
    - Alcohol / drug abuse
- Encourage to join an "*ART Teen Club*" where available. Provide extra support for patients transitioning from a *Teen Club* to the adult clinic.
- Offer condoms; explain use on penis model; give at least 20 condoms
- Explain: Don't have penetrative sex without condom. HIV can travel in semen and vaginal fluid and infect the other person.
- Explain: It is still possible for you to have children when you want to. The risk of passing HIV to your partner or to your baby is very low if your VL is undetectable.
- Explain: Where to access STI treatment, family planning services and help in case of sexual assault.

15.9 Keeping track of months since ART initiation

- Needed to determine when blood samples for routine VL monitoring are to be drawn.
- Calculate and document on the ART patient card the number of months since the patient first started ART. Simply calculate the number of months since first ART initiation, ignoring any potential gaps (periods of stopping / defaulting).
- Electronic medical record systems give automatic reminders when scheduled VL samples are due.

15.10 Monitoring for treatment failure / HIV drug resistance

Key Facts: ART failure and drug resistance

- ARV drug resistance starts gradually and the virus will still be partly suppressed for many months. Emerging drug-resistant virus does not cause any immediate clinical symptoms.
- HIV will grow resistant to more and more ARVs if a patient continues to take a failing ART regimen for several months. Accumulated multiple ARV resistance can make it difficult to find a second line regimen that still works.
- HIV drug resistance usually affects different ARVs of the same class.
- ***Example:*** HIV that has grown resistant to EFV will also be resistant to NVP, even if the patient has never taken NVP before.
- Drug resistant virus can be transmitted to other people.
- ***Example:*** About 10% of Malawians who got newly infected with HIV in 2015/2016 acquired virus with some level of drug-resistance against standard ARVs (MPHIA 2016).

15.10.1 Clinical screening and diagnosis of treatment failure

- **Suspect ART failure** if <u>both</u> of the following clinical conditions are met:
    - On ART for 12 months or more
    - New HIV-related disease / unexplained weight loss / failure to thrive
- For all **suspected ART failure** cases, look for indications for poor adherence in the last 6 months
    - Adherence was good:
        - Do a <u>targeted VL</u> or refer to have this done immediately.
    - Adherence was questionable:
        - Start intensive adherence counselling (see **page 74**)
        - Do a <u>targeted VL</u> after 3 months if adherence was satisfactory.
- See **Figure 5** on **page 80** for the interpretation of VL results.

15.10.2 Viral load (VL) testing

Key Facts: Viral load testing

- VL is the best measure for the level of progression of HIV infection.
    - VL = number of viral particles per ml of blood.
    - More virus ⇨ faster destruction of CD4 cells ⇨ more severe immunosuppression.
- Successful ART leads to such low levels of HIV in the blood that it can no longer be detected with VL testing. An ***undetectable VL*** is also called ***viral suppression***. This is the ***aim of ART***.
- VL testing is expensive.
- VL testing uses an advanced lab method (RNA-PCR) on a blood sample. It can be done from:
    - Dried blood spot (DBS): Transport in plastic bag with desiccant at ambient temperature, sample viable for 3 months or more (see **section 9.4** on **page 38**).
    - Blood plasma: Transport in cooler box to lab within 24 hours.
- VL is required to confirm suspected ART failure (clinical and/or CD4-based).
- Routine VL monitoring is being scaled up gradually.
- The VL schedule is designed to detect ART failure early while avoiding unnecessary tests to save cost:
    - Patients with drug-resistant HIV when starting ART may have a high VL after **6 months** on ART. This can be from infection with drug-resistant HIV or after taking sdNVP. Otherwise, a high VL at 6 months is an important sign for poor adherence.
    - After that, patients who are adherent and well have a low risk of ART failure. Therefore, routine follow-up VLs are done at **2 years**, **4 years**, **6 years**, **etc**. after ART initiation.
- Do additional targeted VLs outside of this schedule when suspecting ART failure.
- Explain the standard VL monitoring schedule to every patient. Ask the patient to help remember when VL is due.
- Actively communicate (phone / home visit) any detectable VL results (above detection limit, even if <1000) to patients as soon as the result is received at the site. Call for an early appointment.

When to do VL

- **Routine scheduled** VL is done for all patients at specific times after ART initiation:
    - At 6 months, 2 years, 4 years, and every 2 years thereafter.
    - Collect catch-up VL sample at the next opportunity if the regular schedule was missed. Continue with the regular schedule (determined by the time since ART initiation).
- **Targeted/Repeat**
    - Routine VL result was detectable and patient has received IAC and 3 months have elapsed since IAC was started.

- Patient with clinically suspected treatment failure and we are confident adherence in the last 3 months was good.
- Mandatory before starting 2nd line ART to confirm suspected ART failure.

Interpreting and acting on VL results

- Review **Figure 5** on **page 80** for indication, interpretation and action from VL testing.

Successful ART

Finding	**Routine** or **targeted / repeat** VL below detection limit
Interpretation	Successful ART
Action	Praise the patient and encourage further good adherence. Continue on the same regimen. Monitor VL at next milestone.

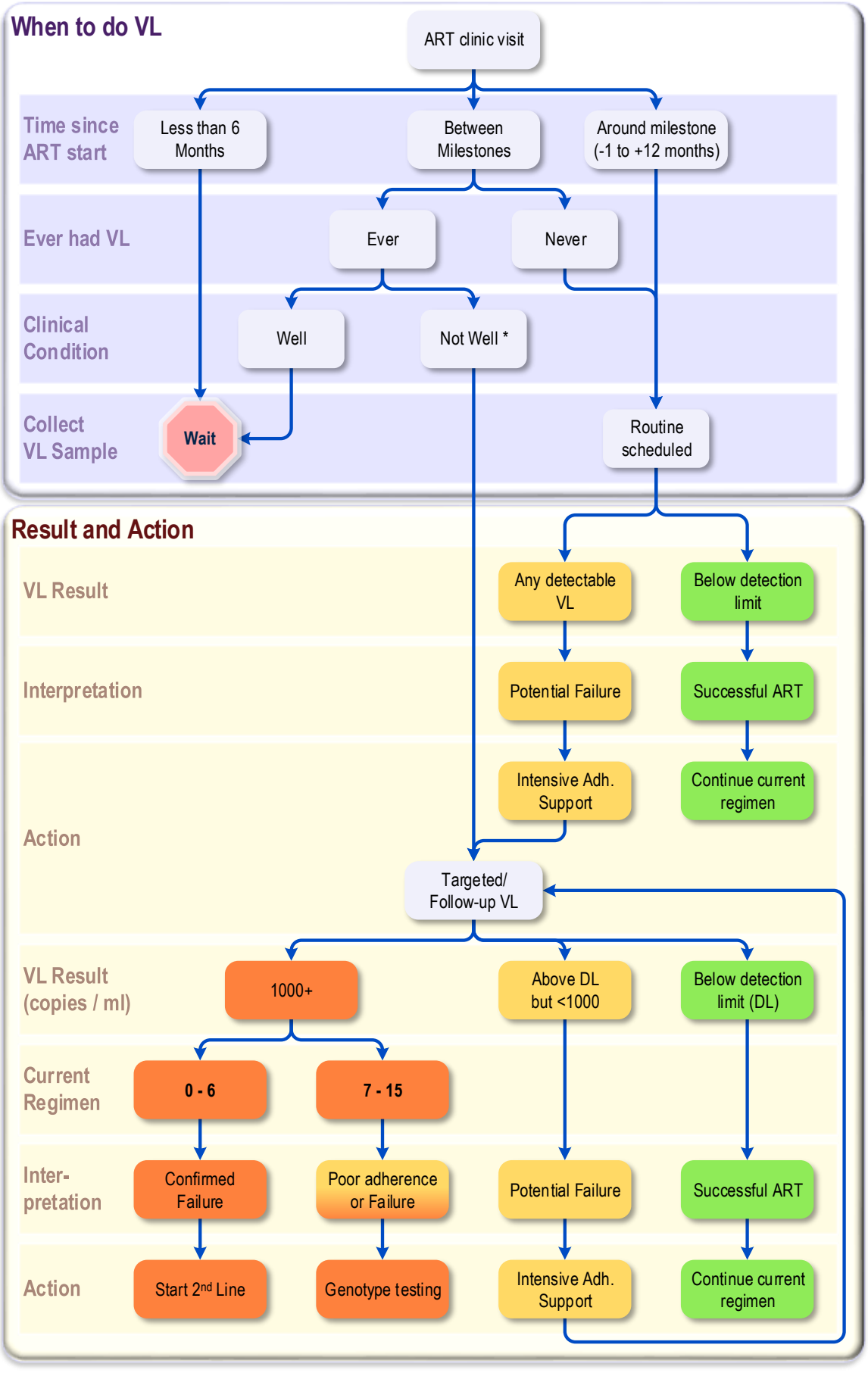
Potential treatment failure

Finding	**Routine** VL result detectable (even if below **1,000**)
Interpretation	Potential treatment failure
Action	Start intensive adherence counselling (see page **74**). Continue on the same regimen. Collect repeat VL after 3 months of good adherence.

Confirmed treatment failure

Finding	**Targeted / repeat** VL result **1,000+** *AND* Patient is **on NNRTI-based regimen (0, 2, 4, 5, 6)** *AND* **good adherence** in the 3 months before sample collection
Interpretation	The virus is likely resistant to the current ART regimen.
Action	Start / continue intensive adherence counselling. Consult certified 2nd Line Prescriber for initiation of 2nd line ART without delay. 'Reset the clock' for routine VL monitoring: 6, 24 months, etc. after switch to 2nd or 3rd line. Note: Patients on **DTG- or PI-based regimens (7, 8, 9, 10, 11, 12, 13, 14, 15)** need genotype testing to confirm resistance before changing regimen. This is because a high VL on these regimens is likely due to adherence problems / poor absorption Consult certified 2nd Line Prescriber to and/or call the HIV Dept. hotline (see page **112**) to organize resistance testing. Request 3rd line ARVs if resistance to 2nd line ART has been confirmed.

Figure 5: Indication, interpretation and action for routine scheduled and targeted VL testing



* Any of the following: Significant unintended weight loss, failure to thrive, new or worsening HIV-related disease (suspected or confirmed)

15.11 Updating follow-up outcome

- Regularly review all patient cards and keep an appointment register to identify patients who are overdue for their appointment as soon as possible.
- Try to contact the patient or the named guardian by phone or by home visit from 2 weeks after the missed appointment. Confirm from ART Patient Card that consent was given for home visit.
    - Patient is alive: counsel to return to the clinic as soon as possible and continue treatment.
    - Patient has stopped, died or transferred out: update outcome and date of outcome on patient card and in register.
- Loss to follow-up ('default'):
    - Patient is overdue for the appointment and is not known to have stopped ART, died or transferred to another facility.
    - Classify as 'defaulted' if the patient has run out of ARVs 2 or more months ago (based on the number of tins given at the last visit).
- Patients who are alive but known to have stopped ART (for any reason) should be classified as 'stopped' and not as 'defaulted'.
- Ask guardians to notify the clinic if an ART patient has died. Bring back the patient health passport and/or ART ID and any remaining ARVs.

Table 16: Symptom-based identification and management of side-effects

Cause (in order of likelihood)	**Diagnosis**	**Primary Management**	**Secondary Management**
Body pains, weakness			
AZT, 3TC	Severe anaemia: Hb <7 g/dl	Stop AZT, consider transfusion	Substitute AZT, continue ART without gap
AZT	Lactic acidosis (LA): shortness of breath, nausea Serum lactate: suspect: 2-5 mmol/l, confirmed: ≥5 mmol/l	*Any suspected LA:* Stop all ART immediately IV fluids, treat at hospital	Don't re-start ART before lactic acid <2mmol/l Can re-start ART with AZT after suspected LA Never give AZT after confirmed LA Can use ABC or TDF containing regimen
Fever			
Onset independent of drugs: Bacteraemia, malaria	FBC, MPs, blood culture, urine dipstick		
Onset within 8 weeks of starting drugs: ABC, NVP, EFV	ABC, NVP or EFV hypersensitivity: Body pains, vomiting, diarrhoea, abdominal pain, sore throat, cough, shortness of breath, rash, jaundice	Any suspected hypersensitivity: Stop all ART immediately, treat at hospital	Do not re-start before symptoms have resolved Never use NVP or ABC again Replace NVP with EFV and ABC with TDF
Slimming: Cheeks, forearms, buttocks, legs (often prominent veins) Fattening: Back of neck ('buffalo hump'), breast, stomach, and waist			
AZT, LPV/r, 3TC, TDF, HIV EFV	Lipodystrophy (from ART / HIV itself)	Reassure patient Substitute likely causative ARV	
Breast swelling / enlargement: one- or both-sided, in males or children			
EFV, ketoconazole, cimetidine, omeprazole, spironolactone, isoniazid testosterone deficiency (HIV), AZT, LPV/r	Gynaecomastia: palpate enlarged breast gland Lipodystrophy: accumulation of fat (from ART / HIV itself)	Reassure patient Substitute EFV with NVP in ART regimen.	Consider surgery for extreme gynaecomastia

Cause (in order of likelihood)	**Diagnosis**	**Primary Management**	**Secondary Management**
Upper GI symptoms: Nausea, vomiting			
AZT, LPV/r, 3TC, DTG	Lactic acidosis ? (see '*Body pains and weakness*') Jaundice? (see 'Yellow eyes')	Adults only: Promethazine 25 mg up to 12-hourly. Adults or children (lower dose): Chlorpheniramine (Piriton) 10 mg up to 8-hourly-oral rehydration solution(ORS)	If no lactic acidosis: try to continuing the same ART regimen If persistent, substitute
Skin Rash			
Onset before starting drugs: Seborrhoeic dermatitis ("bumpy itch")	HIV-related skin rash	Adults only: Promethazine 25 mg 12-hourly Adults or children (lower dose): Chlorpheniramine (Piriton) 10 mg 8-hourly Calamine lotion	Consider scabies, etc.
Onset within 8 weeks of starting drugs: NVP, ABC, Cotrimoxazole, EFV	Mild hypersensitivity Macular/papular rash not involving mouth, eyes, and genitalia No fever, body pain, weakness, etc.	Continue EFV, reassure: initial rash mostly resolves. Continue on half dose NVP (if on NVP starter pack) for further 2 weeks Adults only: Promethazine 25mg 12-hourly Adults or children (lower dose): Chlorpheniramine (Piriton) 10 mg 8-hourly	If no improvement on half dose NVP, stop NVP Substitute to EFV once rash has resolved. If patient unable to take EFV, consult with ART specialist for alternatives
Lower GI symptoms: Diarrhoea, lower abdominal pain			
Onset before ART initiation: HIV-induced	Stepwise empirical treatment	Stepwise empirical treatment of chronic HIV diarrhoea (see page 24)	
Onset within 6 weeks of starting drug: LPV/r, AZT, 3TC, DTG	Drug toxicity	For adults only: Loperamide 2 mg 8-hourly (mainly for LPV/r induced diarrhoea)	Try to continue same ART regimen If persistent substitute

Cause (in order of likelihood)	**Diagnosis**	**Primary Management**	**Secondary Management**
Severe upper abdominal pain, nausea and vomiting			
3TC	Pancreatitis Serum amylase >1.5 times above upper normal limit	Stop all ART immediately Treat at hospital	Restart ART after complete remission Use TDF- or AZT-containing regimen
NVP, EFV, alcohol, viral hepatitis	Acute fulminant liver failure Liver function tests	Discontinue ART immediately Treat at hospital Identify cause and manage accordingly	Never re-start NVP or EFV if this was the suspected cause Reinitiate ART one month after jaundice is resolved, and LFT <2.5 of upper normal limit
Yellow eyes			
Viral hepatitis, alcohol, ATV/r, NVP, INH, EFV, ABC, severe malaria, cancer	LFT and ultrasound scan to differentiate: Viral hepatitis, cirrhosis, drug hepatitis, primary liver cancer, metastases	Discontinue ART and IPT immediately if jaundice develops after start. See footnote 13 on page 52 for patients on ATV/r. Identify cause and manage accordingly (LFT, ultrasound, hepatitis serology).	Never re-start NVP or EFV if this was the suspected cause. Re-initiate ART 1 month after jaundice has resolved and LFT <2.5 times upper normal limit.
Swollen face and eyelids, particularly in the morning/tiredness, too much or too little urine			
Onset before starting drugs HIV, diabetes, hypertension	Confirm nephropathy with serum creatinine	Identify cause and manage accordingly	Adjust ART dosage according to creatinine clearance
Onset within 1 year of starting drugs: TDF, streptomycin	Confirm nephropathy with serum creatinine	Admit to hospital Substitute TDF to AZT without gap Stop streptomycin	Adjust ART dosage according to creatinine clearance

Cause (in order of likelihood)	**Diagnosis**	**Primary Management**	**Secondary Management**
Drowsiness, confusion, nightmares, insomnia, psychosis			
EFV, DTG	Neuropsychiatric EFV or DTG toxicity	Drowsiness/ bad dreams usually disappear after a few weeks without the need to discontinue ART. Take EFV before bed. Take DTG in the morning. Confusion / psychosis: replace EFV with NVP immediately	If intolerable beyond 2 weeks: replace EFV with NVP replace DTG with EFV or NVP
Leg pain, numbness or burning, inability to walk			
Onset before starting drugs: HIV neuropathy Onset or worsening after starting drugs INH, vincristine Onset independent of drugs Alcohol, diabetes	Mild peripheral neuropathy (PN): no sleep disturbance	Amitriptyline 25 mg nightly for 4 weeks Pain control using WHO analgesic ladder	If no improvement after 4 weeks: stop amitriptyline, continue analgesics
	Moderate PN: sleep disturbance	Stop responsible drug WHO analgesic ladder	
	Severe PN: severe pain, muscular weakness		

15.12 Immune reconstitution inflammatory syndrome (IRIS)

Key Facts: IRIS

- A small number of patients may get worse in the first 6 months after starting ART.
- The most common causes for this are (in the order of likelihood):
    - Undiagnosed / untreated OI, mainly TB
    - Poor adherence to ART
    - Drug-resistant TB (if on TB treatment)
    - IRIS
- IRIS is an over-aggressive response of the immune system caused by a sudden recovery on ART.
- IRIS appears as a severe bout / worsening of an OI:
    - TB
    - Cryptococcal meningitis
    - Herpes zoster
    - KS
    - Hepatitis
- IRIS should only be considered if the more common causes for worsening have been ruled out.
- Patients who start ART with very advanced AIDS are at a higher risk of developing IRIS.
    - Recent / concurrent treatment for TB or cryptococcal meningitis.

15.12.1 Management of IRIS

- Confirm that ART is actually taken as prescribed.
- Continue ART if ART toxicity has been ruled out as the underlying cause.
- Treat the OI.
- Consider TB treatment failure if worsening occurs after more than one month on TB treatment.
- Admit severe cases to hospital.
- Seek specialist advice on whether NSAIDs and/or prednisolone should be given.

16 Differentiated ART services

Key Facts: Differentiated ART services

- Differentiated ART Service Delivery (DSD) is a patient-centred approach that adapts continuum of HIV services to the individual needs of PLHIV.
- DSD is promoted by WHO to improve the quality of care of the growing number of PLHIVs across the ART clinics.
- DSD tailor interventions based on the individual patient clinical need by reducing the burden of unnecessary clinical visits as well as helping the ART service provider prioritize additional care the patient may require.
- The choice of specific DSD model should be based on feasibility, affordability and clear benefit, to the patient and the health system
- Commonly, differentiation of HIV care & treatment services delivery aim to cater for the varying needs of stable and unstable patients on ART.
- DSD clinics must have all patient information linked to the national data stream
- Please, refer to specific SoPs for individual DSDs.

- Standard operational definition of stable patient:
    - On the current ART regimen for 12 months+ without any side effects
    - No obvious opportunistic infections that could compromise ART
    - Latest VL within the last 24 months was below detection limit
    - Not pregnant or breastfeeding
- Stable patients may be scheduled into approved MoH DSD models, including Teen Clubs, mobile clinics like ART-provider managed Community ART Groups, DHO-linked Drop-in-Centres, 3-multi-month prescription and pharmacy fast-track refills.
- Standard operational definition of unstable patients (advanced illness) or patients at high risk of disease progression
    - Latest VL result above detection limit
    - WHO Clinical Stage 3 and 4
    - CD4 count of 200 and below
- See sections **8.1** (**page 22**) and **15.10** (**page 77**) for management of patients with advanced illness or at risk of disease progression. Patient with advanced illness must managed within the clinic settings.

17 Management of labour and delivery

17.1.1 HIV status ascertainment at maternity

- Review HIV testing page in health passport on admission.
- Provide **new HIV test**[20] for all women, who are:
    - Not already known to be HIV positive
    - Never tested or tested negative any time in the past, even if this result is from the last trimester.

17.1.2 ART provision at maternity

- Mothers already on ART: continue the same ART regimen at regular prescribed intervals. Pregnancy / breastfeeding are no indication to change women from any previous ART regimen.
- HIV positive mothers not yet on ART / who interrupted / stopped ART: emergency ART initiation
    - Start lifelong TDF/3TC/EFV (Regimen 5A) as soon as possible, during labour or after delivery.
    - Deliver individual ART counselling and IEC before discharge.

17.1.3 Reduce obstetric risk of HIV transmission

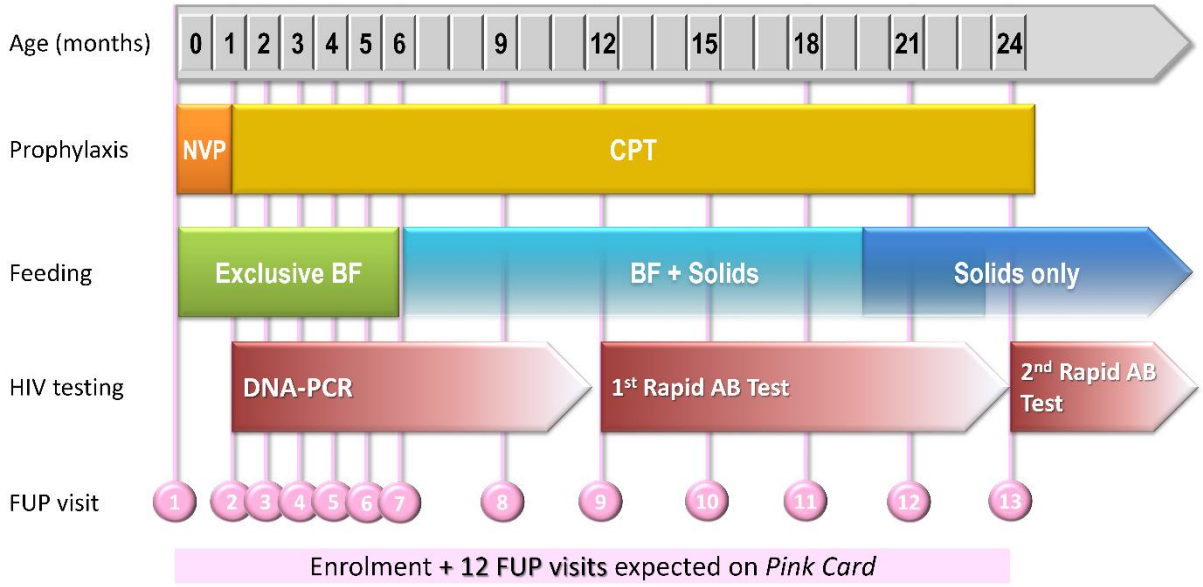
- Use a partogram to allow early detection and management of prolonged labour.
- Artificial rupture of membranes (ARM) increases the risk of HIV transmission.
    - ARM is not indicated if labour is progressing well.
    - If prolonged labour due to poor uterine contraction: perform ARM at ≥6cm cervical dilation and augment with oxytocin (pitocin).
- Do not perform routine episiotomy except for specific obstetric indications (e.g. vacuum extraction).
- Avoid frequent vaginal examinations.
- Do not 'milk' the umbilical cord before cutting.
- Do not suction with a naso-gastric tube unless there is meconium-stained liquor.
- Immediately after birth, wipe the baby dry with a towel to remove maternal body fluids.

20 There is no general time limit for offering HIV testing. Consider that other important interventions such as C-section or tubal ligation are also offered with emergency counselling very late in labour.

18 New born care and postnatal follow-up

- Follow regular post-natal care.
- Give all regular EPI vaccinations to all babies born to HIV infected mothers (as for all other infants).
- See **Figure 6** below for the standard schedule of HIV exposed child follow-up: NVP prophylaxis, CPT, feeding and HIV testing

Figure 6: Standard follow-up schedule for HIV exposed children



18.1 Initiating integrated mother/infant follow-up

- Ensure continued follow-up for HIV infected mothers and babies.
- Enrol baby in HCC before discharge from post-natal ward:
  - Fill Exposed Child patient card, enter in HCC register.
- Mothers on ART before delivery:
  - Confirm next ART appointment.
  - Synchronise mother's ART appointment with baby's first HCC visit. Aim for first HCC visit at post-natal visit or first vaccination visit.
- Mother initiated ART in labour:
  - Fill ART patient card and enter in ART register.
  - Write baby's HCC registration number on mother's ART card.
  - Give regular 4-week ART + HCC appointment.
- If mother wants to continue HCC and ART at another facility:
  - Record 'transfer out' in HIV clinic and ART register and give mother her ART patient card and the baby's Exposed child card.

18.2 Infant and child feeding counselling

Key Facts: HIV-exposed child feeding

- Feeding recommendations are the same for all infants, regardless of HIV exposure or HIV infection status.
- Give only breast milk up to age 6 months.
- Gradually start complementing breastfeeding with suitable hygienically prepared foods from age 6 months (such as Likuni Phala, fruits, vegetables, beans, ground nuts and soya).
- Aim to stop breastfeeding around age 22 months, so that the final HIV test can be done at age 24 months (6 weeks after breastfeeding has stopped).
- Stop breastfeeding gradually over a period of 1 month (no *rapid cessation*).

- Replacement feeding (formula) is **NOT** recommended unless women are unable to breast feed.
- Monitor weight, height and MUAC according to schedule using standard MOH charts and intervene if no adequate weight-gain.
- Give only medicines prescribed by a health professional.
- Start breastfeeding immediately after birth. Explain and observe optimal breastfeeding:
    - Empty both breasts properly to avoid breast engorgement.
    - Ensure proper attachment and positioning to minimize nipple cracks and fissures.
    - Watch out for signs of breast infection (pain, swelling, heat, redness)
        - Don't feed baby from infected breast. Express infected breast to avoid engorgement. Discard expressed milk – do not feed to baby.
        - Go to health facility for treatment. See **section 12.2.8, page 288** in the Malawi Standard Treatment Guidelines (**MSTG 2015**, 5th Edition)

18.3 Infant NVP prophylaxis

Key Facts: Infant nevirapine prophylaxis

- NVP syrup is given to all babies born to HIV infected mothers.
    - NVP syrup shields the baby from HIV infection during the most risky time.
    - Give NVP syrup to the baby 24-hourly for 6 weeks.
    - All babies should take NVP syrup for the same duration regardless of the mother's ARV regimen and regardless if the mother was taking ARVs at all.
- Store NVP syrup bottles and syringe: dark, cool, clean and dry and out of children's reach.
- Use an old syrup bottle filled with water to show how to draw 1.5ml of syrup in the syringe.
- Hand out one example syringe where the 1.5ml line has been marked with a pen.
- Squirt the syrup in the back of the infant's mouth between the cheek and the gum to ensure it gets swallowed (use cup to demo).
- Rinse the dosing syringe carefully with clean water after every use and let dry.
- Bring back to the health facility at the 6 week vaccination visit all NVP bottles (whether used or unused). The nurse will check if the right amount was used.

18.3.1 Prescription and dispensing of NVP prophylaxis

- When to dispense NVP syrup for infant prophylaxis to take home:
    - At ANC (or maternity) as soon as the mother is known to be HIV-infected.
    - Unopened bottles of NVP syrup have a long shelf-life. Therefore, never delay dispensing until later in pregnancy. Make sure the expiry date is at least 2 months after the estimated delivery date.
    - Ask at every following visit if the NVP syrup and the syringes are still available. Replace without delay any items that may have been lost or spoilt.
- Dispense **2** x 100ml-bottles of NVP syrup with dosing syringe.

18.3.2 Dosing

- The dose of NVP syrup remains the same for the whole 6-week period – do not change the dose according to age or body weight, etc.
- Use the standard dose (1.5ml) If birth weight is unknown (home birth / no scale).

Table 17: Dosing of NVP syrup for infant prophylaxis

Birth weight	NVP syrup (10mg per ml)
2500g or less	**1.0 ml** 24-hourly
Over 2500g / unknown	**1.5 ml** 24-hourly

18.3.3 Timing and duration

- Start giving NVP syrup as soon as possible after birth. The earlier the start, the more effective.
- NVP syrup can be started anytime between birth and 4 weeks of age if the mother presents late. Starting NVP prophylaxis later is less effective and may cause drug-resistant HIV if the baby is already infected (and needs to start ART).
- Stop giving NVP syrup when the infant is 6 weeks old. The infant will receive less than 6 weeks of prophylaxis if NVP syrup has been started late.

19 Transition to new ART regimens (2018/2019)

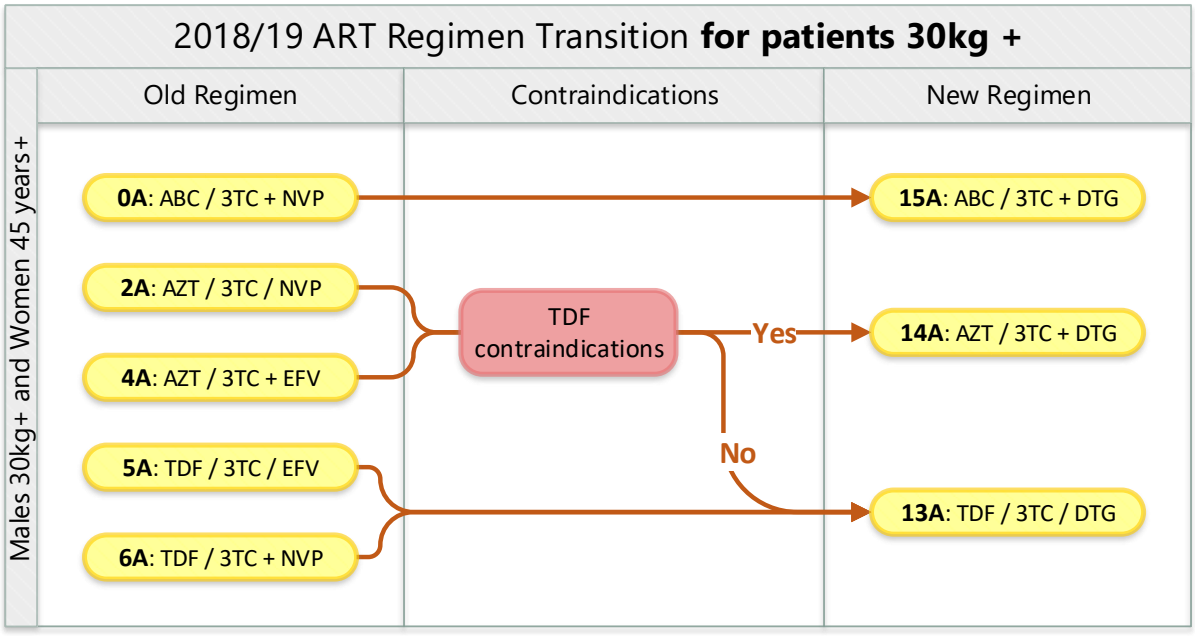
19.1 New ART initiation / re-initiation after gap

- Use **Table 10** on **page 48** to select the right start regimen for the respective patient.

19.2 Transition for patients currently on ART

- **Figure 7** on **page 93** shows which patient groups should routinely change to a new regimen **once stocks of the new regimens have arrived** at the site.
    - Check current weight for all patients before transition to **13A, 14A** or **15A**: weight must be 30kg and above. There is no age restriction for children from 30 kg.
    - Patients should use up their previously dispensed ARVs before changing to the new regimen.
    - Patients on any other regimen not listed in **Figure 7** remain on their current regimen unless there is a specific indication to change.
- Explain to all patients the information from *Key Facts: Dolutegravir* on **page 46**.
    - Advantages
    - Potential side effects
    - Contra-indications
    - Drug interactions: especially not to take at the same time as multi-vitamins, FeFo, antacids, etc.
- **0A**, **2A**, **4A**, **5A** and **6A** will remain available as alternative regimens for patients with specific conditions / contraindications.

Figure 7: ART regimen transition for males with current weight 30 kg+ and women 45 years+



20 Pre-exposure prophylaxis (PrEP)

Key Facts: Pre-exposure prophylaxis

- Although HIV negative people who are at very high risk of getting infected with HIV can benefit from PrEP, significant implementation challenges have limited the effectiveness in comparable settings.
- PrEP uses daily TDF/3TC or TDF/FTC tablets.
- Is not approved for roll-out as a public health intervention for HIV prevention in Malawi.
- PrEP acceptability and retention are currently being evaluated by MOH approved implementation research.
- Gathered evidence will help guide future guideline revision.

21 Post exposure prophylaxis (PEP)

Key Facts: Post-exposure prophylaxis

- HIV infection can be prevented after a high risk contact with fluids from an HIV infected person.
    - Remove immediately as much as possible of the body fluid.
    - Immediately give a 3-day supply of PEP and start taking it as soon as possible.
    - Assess risk and test for HIV as soon as possible. Continue a 30-day course of ARV prophylaxis (PEP) if exposure is classified as 'risk' and exposed person is HIV negative.
- PEP, if taken correctly, reduces the risk of infection by 80%.
- ARVs taken for PEP are usually well tolerated.
- Keep ARVs for PEP accessible 24/7, e.g. at maternity or other well-advertised locations.
- Offer STI treatment and emergency contraception, for rape victims accessing PEP.
- The risk of getting infected may be high or low, depending on the type of substance and contact. However, PEP should always be started if there is a possible risk of transmission (see classification in **Table 18** on **page 95**).

Classification of risk

- Use **Table 18** to find out if the exposure is a possible risk for infection.
- Obtaining a new HIV test from the source person can help to reassure that the risk is low, but PEP should still be given if the test result is negative. The source person could be newly infected himself and may be in the window period.

Table 18: Classification of risk of transmission after exposure to HIV

	Substance	Type of contact	Source person
Risk	• Blood • Semen • Vaginal fluid • Cerebro-spinal fluid • Pleural fluid • Amniotic fluid • Synovial fluid • Ascites fluid	• Skin penetrated with contaminated needle (hollow or non-hollow) • Large amount of substance on mucous membrane • Sexual intercourse no condom • Risk substance on lacerated skin / open wound	• Regardless of known/unknown HIV status
No Risk	• Urine • Stool • Pus • Tears • Saliva • Sputum • Nasal secretions	• Risk substance on intact skin	

Immediate measures

- Remove infectious substance.
    - Wash exposed wounds and skin sites thoroughly with soap.
    - Flush mucous membranes with water.
    - Do not use bleach, antiseptics or other caustic substances.

Eligibility to start PEP (ARV prophylaxis)

- Any exposure classified as risk in the last 72 hours (see **Table 18**).
- Never refuse PEP on moral judgement about the kind of exposure (accident, negligence, rape, 'burst condom').
- New HIV test is mandatory to confirm negative HIV status,
    - BUT: Don't delay starting PEP if HIV testing is not immediately available (no test kits, night, etc.). Do HIV testing as soon as possible.
- PEP is safe in pregnancy and breastfeeding.
- Severe anaemia (<8g/dl) is contraindication for AZT/3TC.
- Severe renal failure is contraindication TDF/3TC.

How to start PEP

- Start taking PEP as soon as possible after high risk exposure, ideally within 2 hours.
- Starting PEP more than 72 hours after exposure is not effective and should not be done.
    - However, still perform HIV testing at baseline, at 3 and 6 months.
- Explain dosage and importance of adherence.
- Mild side effects (nausea, etc.) are not a reason to stop PEP.
- Advise to return immediately if serious side effects are suspected.

- Advise all exposed adults to practice safe sex until confirmed HIV negative at 3 months.
    - Give 30 condoms and re-supply as requested.
- Do not stop breastfeeding.
- Write case details in PEP register (improvised).

Table 19: Post exposure prophylaxis regimens and dosage (number of tabs taken)

	Standard						Alternative			
	AZT 60mg / **3TC** 30mg		**AZT** 300mg / **3TC** 150mg		**TDF** 300mg / **3TC** 300mg / **DTG** 50mg		**ABC** 60mg / **3TC** 30mg		**AZT** 300mg / **3TC** 150mg	
Weight										
3.0 – 5.9 kg	1	1					1	1		
6 – 9.9 kg	1½	1½					1½	1½		
10 – 13.9 kg	2	2					2	2		
14 – 19.9 kg	2½	2½					2½	2½		
20 – 24.9 kg	3	3					3	3		
25 – 29.9 kg			1	1					1	1
≥ 30.0 kg					1	0			1	1

PEP follow-up

- At 30 days: (after completing ARV prophylaxis)
    - Assess adherence
    - Give 60 condoms
- At 3 months and 6 months: repeat HIV testing

Additional prevention measures after rape / sexual exposure

- Give emergency contraception (EC) within 72 hours if needed (see **Table 20**)
    - Repeat dose if vomiting occurs within 1 hour of taking EC.
    - Explain that next menstrual period should occur before or around the expected time.
- Consider giving presumptive treatment for STIs using **Table 21**
- Follow *National Guidelines for Provision of Services for Physical and Sexual Violence (2015)*

Table 20: Regimens and dose for emergency contraception

Contraceptive drug	Immediately	After 12 hours
Postinor 2 (750µg levonorgestrel)	2 tablets	
OR		
Lo-Feminal or Microgynon	4 tablets	4 tablets

Table 21: Dosing of standard presumptive STI treatment after sexual exposure

STI drug	Child <15 years	Adult
Benzathine pen. vials	50,000 IU/kg IM stat (max 2.4 million IU)	2.4 Mega Units IM stat
Gentamicin vials	7.5 mg/kg IM stat (max 240mg)	240mg IM stat
Erythromycin tabs	12.5 mg/kg 6-hourly for 14 days (max 500 mg per dose)	500mg 6-hourly for 7 days
Metronidazole tabs	5 mg/kg 8-hourly for 7 days (max 2 g per day)	2g stat
Nystatin pessaries	N/A	100,000 units 12 hourly for 7 days

22 Pharmacovigilance

Key Facts: Pharmacovigilance

- Pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems.
- Adverse drug reactions (ADRs) can be detected by either a patient or guardian or health care practitioner.
- Report all ADRs (minor and serious) that are a concern to either a patient or guardian (e.g. persistent fever) and to the health care provider (e.g. jaundice).
- All ADRs should be reported within 48 hours using a standardized reporting tool, **ADR Reporting Form (Version 1.1)**. Serious ADRs (e.g. death) must be reported within 24 hours.
    - Adverse drug reactions are considered serious if they result in any of the following: death; life-threatening; disability; hospitalization/prolonged hospitalization; congenital anomaly; require intervention to prevent impairment/damage and; any other important medical event.
- The Pharmacovigilance Center is based at the Pharmacy Medicines and Poisons Board (PMPB), and all reports are collected and aggregated by them. Reports concerning with PLHIV are shared with DHA.

22.1 How to fill in the ADR Reporting Form

- All sections of the form must be filled in with adequate details. The following basic information is required before the form is acceptable:
    - Identifiable source of information or reporter
    - Identifiable patient
    - Name(s) of the suspected product(s)
    - Description of the suspected reaction
- The form contains the following 5 sections:
    - Fill in section 1 with the Patient Information for example name, age, DOB and gender.
    - Section 2 contains information of the Adverse Event. Key areas include the date of onset and brief description of the ADR as well as action taken (e.g drug withdrawn or dose reduced). If any laboratory tests have been conducted to investigate the ADR, these must also be filled in with their results. If the outcome is death the date of death must be indicated.
    - Section 3 provides information of the suspected drug that caused the ADR. Both the generic and brand name as well as batch number should be indicated.
    - Indicate in section 4 other drugs including herbal remedies that were taken prior to the ADR.

- The reporter's information must be indicated in section 5, in order for PMPB and DHA to be able to follow up on the case should more information be required.

22.2 How to handle serious ADRs

- Any serious adverse event should be reported immediately to the next level using the easiest and fastest mode of communication for example phone call, email, SMS. This should be followed by a written report that must be sent within 24 hours of the event occurring.
- Serious ADRs will be investigated by a qualified team and the report will be shared to the PMPB, DHA as well as reporting site.

23 Monitoring and evaluation

Key Facts: Monitoring & Evaluation

- The HIV program relies heavily on accurate and timely data for planning, reporting to donors and for drug procurement and distribution.
- Data analysis and reporting is done from patient cards and clinic registers at most facilities, but electronic systems for monitoring are used at sites with many patients.
- Reporting is done monthly for ANC, maternity and exposed child follow-up and quarterly for ART (see Table 22 on page 103)
- Cohort analyses are needed to report outcomes of patients in ANC, exposed child and ART follow-up. Cohort reports look at the current / latest status of all patients enrolled in follow-up and require a review of all patient records to classify primary and secondary outcomes before data can be aggregated for reporting.
- Reports from facilities are to be completed within 5 working days after the end of the reporting period.
- HIV Program reporting will be further integrated into the regular Health Management Information System. Monthly / quarterly facility reports will be entered directly into the District Health Information System at the District Health Offices for national reporting.

23.1 Definitions

PMTCT site

- A facility is counted as a PMTCT site if they have initiated on ART at least one pregnant or breast feeding woman during the reporting period.
- Depending on the mode of integration of PMTCT/ART interventions into the general health services, ART may be initiated in any of the following service points: ART, ANC, maternity, post-natal or under 5 clinic.

ART site

- A facility is counted as an ART site if they had retained at least one patient alive on ART at the end of the reporting period.

ART status at registration

- Refers to the patient's status at the time of first registration at this ART clinic – this status will never change as long as the patient remains at this clinic.
- **First time initiation:** Never taken ART (triple ARV combination treatment) in the past. Having taken ARVs for prophylaxis (PEP, single dose nevirapine, AZT combination prophylaxis for PMTCT) does NOT count as having taken ART and is ignored for the *ART status at registration*.

- **Re-initiation**: Received ART (triple ARV combination for treatment) from another ART site in the past but has NOT been taking it for 2 weeks or more as of the day of registering at this clinic. Patients who have interrupted for 2 weeks or more need to take a starter pack for re-initiation (if started on a regimen containing NVP).
- **Transfer in**: Received ART from another ART site in the past and is currently taking ART or has interrupted for less than 2 weeks. Count as *Transfer In* regardless if the patient brings his old patient card or not ('official' or 'unofficial' transfer).

Defaulted / Lost to follow-up

- Patients are counted as 'defaulted' in the cohort report if they have not returned to the clinic and are not known to have transferred out, stopped or died.
- The following times apply in the different clinics:
    - HCC (HIV exposed children): 2 months after the *Next Appointment Date* given at the last visit.
    - ART: 2 months after the patient is expected to have run out of ARVs.
- Patients may revert to 'alive on ART' when the next cohort analysis is done if they return to the clinic and continue ART.

ART stop

- Patients are counted as 'stopped' if they are last known to be alive and have stopped taking ART. Stop is used regardless:
    - Of the reason the patient has stopped (clinician's or patient's own decision).
    - If the ART interruption is intended to be permanent or temporary.
    - Of the duration of the ART interruption at the time of doing the cohort analysis.
- Patients may revert to 'alive on ART' at the next cohort analysis if they re-start ART.

Died

- Patients are counted as 'died' if there is a reliable report about the patient's death. 'Died' is used regardless:
    - Of the cause of death (HIV- or non-HIV related disease, accident, suicide or homicide).
    - If the patient was on ART or not at the time of death.

ART re-start

- Interrupted ART for more than 2 months while registered at the respective ART site. Update the number of re-starts in the ART clinic register whenever the patient re-started ART after defaulting or stopping for more than 2 months (i.e. returns after 'defaulting'). Patients who have interrupted for 2 weeks or more need to take a starter pack for re-initiation (if started on a regimen containing NVP).

ART adherence level

- Reporting of adherence levels is based on a classification of the number of doses missed at the last visit before the end of the quarter evaluated.

- The translation of the number of doses missed into adherence % depends on the number of days since the last visit. In practice, it is too complicated to consider varying intervals when analysing cohort adherence. Therefore, 2 monthly visits are assumed for all when classifying adherence for reporting.
- Patient who are supposed to take 1 tablet per day (e.g. Regimen 5A) and who have missed more than 3 tablets are classified as 'less than 95% adherent'.
- Patients who are supposed to take 2 tablets per day (e.g. Regimen 1A) and who have missed more than 6 doses are classified as 'less than 95% adherent'.

Table 22: Overview of M&E systems for integrated HIV program reporting

Service	M&E tools		Report cycle	Report elements			
	Patient card	Register		New registrations	Cohort outcomes		
					Definition of cohort	Primary outcomes	Secondary outcomes
ANC	–	ANC Clinic Register	Monthly	New first visits	• Registration group (6 months after first ANC visit)	–	(Final status at end of ANC) • HIV test status • On ART
Maternity	–	Maternity Register	Monthly	New deliveries	–	–	–
ART	ART Patient Card (separate cards for paediatric and adult formulations)	ART Clinic Register	Quarterly	Patients newly registered at ART clinics	• Cumulative (all ever registered) • Registration group (survival analysis)	• Alive on ART • Died • Defaulted • Stopped ART • Transferred out	• ART regimen / formulation • Adherence level • Side effects • TB status • On CPT • Using FP
Exposed child FUP	HIV Care Patient Card, Exposed Child Under 24 Months	HIV Care Clinic Register	Monthly	Patients newly registered at HCC	• Birth cohort: children who (would) have turned 2, 12 and 24 months of age	• Alive in exp. child FUP • Discharged uninfected • Started ART • Defaulted • Transferred out • Died	• Age when received DNA-PCR result • Latest HIV status

23.2 Reporting of registration data

- For all new patients registered, baseline data (such as age at registration, sex, pregnancy status, clinical stage, etc.) are recorded on patient treatment cards and copied into the clinic register.
- These details do not change over time and tallying of these data needs to be done only once when reporting on new patients registered during the reporting month or quarter.
- *Page summaries* in the clinic registers are filled as soon as each page is full. Count the number of circled values for each column on the page.
- **Monthly** or **quarterly registration reports** are obtained by adding the page summaries from each page in the respective reporting month or quarter.
- **Cumulative registration reports** are obtained by adding the data from the new monthly or quarterly registration report to the data from the previous cumulative registration report.
- Data elements in most sections should add up to the respective total number of patients registered.
    - Males, non-pregnant females and pregnant females must add up to the total number registered.
    - Age groups must add up to the total number registered.
    - ART status (first time initiations, re-initiations, and transfer ins) must add up to the total number registered.
- Some registration data (such as the number of patients with KS at the time of ART initiation) are counted separately and are not part of a section. These data elements are not expected to add up to the total number registered.

23.3 Reporting of cohort outcomes

- *Cohort analyses* are needed to measure outcomes of patients in follow-up.
- In principle, the outcome status of any patient ever registered can change at any time, unless they have died. Therefore, the records of all patients ever registered have to be reviewed each time a cumulative cohort outcome analysis is done. Current outcome data cannot be obtained by addition from the previous quarterly outcome data.
- Patient outcomes are considered as of the last day of the reporting period. Any events (e.g. death) that happened after that day are ignored in the respective cohort analysis, but will be counted in the next report.

Primary follow-up outcome

- The primary outcome shows if a patient has been retained alive in care or if he has dropped out and why.
- The primary outcome categories must add up to the total patients registered in the cohort.
- **Table 22** lists the primary follow-up outcomes used for the different reports.
- For ART only, deaths are further classified according the time after ART initiation. The categories used are: death within 1st, 2nd, 3rd month after ART initiation or after 3rd month of ART initiation.

Secondary outcome

- Secondary outcomes are the latest treatment details among the patients retained alive in care.
- Secondary outcomes are counted directly from the cards of the patients retained alive in care, usually by looking at the last visit before the end of the month or quarter evaluated. This visit might be several months before the end of the quarter, for example if the patient is on long ARV dispensing intervals (as long as the patient is still classified as 'retained alive in care' at the end of the quarter evaluated).
- Each set of secondary outcome categories must add up to the total number of patients retained alive in care.
- **Table 22** shows the secondary outcomes used for the different reports

Definition of cohorts for different program reports

- 3 slightly different methods are used to define cohorts for outcome analyses:
- **Cumulative cohort** (ART): Follow-up status of all patients ever registered at the respective clinic. The number of patients with adverse follow-up outcomes (death, default, etc.) inevitably increases over time. The number of patients retained in care is calculated by subtracting all patients with adverse follow-up outcomes from the total patient ever registered.
- **Registration group cohort** '*Survival analysis'* in ART: Follow-up status of patients registered during the quarters that ended 12, 24, 36, 48 and 60 months ago (ART). *ANC cohort outcomes:* final status as of the last ANC visit for the women who started ANC 6 months ago. This method standardises follow-up times and makes outcome data comparable between sites and over time.
- **Birth cohort** (HIV exposed child follow-up): Follow-up status of children who (would) have turned 2, 12 and 24 months old. Patient cards are filed in batches by month and year of birth (birth cohorts) and only the cards of children born 2, 12 and 24 months ago are pulled out for reporting. Outcomes are counted separately for the 2-, 12- and 24-month birth cohort. Reporting is done monthly and a different birth cohort is covered in each reporting month. This method standardises ages and is used for children enrolled in HIV exposed child follow-up.

23.4 Record keeping and filing

Confidentiality of patient records

- All patient cards and clinic registers are property of the MOH and may only be kept at the respective facility or at the National Archives.
- Patient cards and clinic registers must be kept in a locked room and are only to be accessed by clinic staff responsible of providing the respective service and by the national supervision team. Patients and named guardians have access to their own patient card.

Use of clinic registers (ANC, Maternity, HCC, ART)

- Keep patient registration for each different service centralized in each facility: Use only one set of registers in each facility.
- Each patient has only one row[21] in each register: Continue using the same row for returning transfers and re-starts after default or stop.

[21] In the ANC register, each woman has one separate section with rows for each subsequent visit.

- Turn to a new page when starting to register patients in a new quarter. Leave any unused rows at the bottom of the previous page empty. This is to separate the quarters when adding page totals.
- Assign continuous registration numbers (by sequence of registration). Take care not to duplicate registration numbers.
    - Continue assigning cumulative registration numbers in the HCC- and ART-Register. These number series are never re-started.
    - Re-start assigning registration numbers annually for the ANC- and Maternity Register. Re-start with number 1 on the 1st of July.

Use of patient cards

- Each patient has only one patient card at any one time (Exposed child, ART). Attach another patient card once the old card is full.
- Patient cards are filed in polythene sleeves in lever arch files, up to 100 cards per arch file.
- Separate filing systems are used for the different types of patient cards:

Exposed Child under 24 Months cards

- File in batches by year and month of birth.
- Within each birth month, sort in ascending order by HCC registration number.
- Do not remove the cards of children who have started ART, died, defaulted or transferred out from this filing system.
- Files with birth cohorts who (would) have now reached at least age 3 years can be removed from the clinic for archiving.

ART Patient cards, paediatric and adult ARV formulations

- File ART Patient Cards in ascending order by ART registration number.
- Prepare separate filing systems for **ACTIVE** (retained in ART) and **INACTIVE** patients (stopped ART, transferred out, defaulted, died).
- One arch file can hold approximately 100 cards.
    - Label the **ACTIVE** files with ART numbers 1-100, 101-200, 201-200, etc.
    - Label the **INACTIVE** files with ART numbers 1-200, 201-400, 401-600, etc.
- Each time the quarterly cohort analysis is done, update in the ART register the outcome for patients who have dropped out of ART (stopped ART, transferred out, defaulted or died). Straight after this, move these cards of from the **ACTIVE** to the **INACTIVE** filing system.
- Do not separate **paediatric** and **adult ARV formulation** cards into different files.

23.5 Ensuring adequate data quality

- Use only the standard national reporting forms.
- The clinic's own reports are checked by the supervision team each quarter from primary records.
- Copies of the checked reports are kept at the clinic.

24 Supply Management

Key Facts: Supply Management

- The HIV program requires an uninterrupted supply of huge amounts of very expensive drugs and lab supplies.
- Commodity stock-outs lead to an interruption of life-saving health services. ARV stock-outs are especially serious because patients who interrupt treatment can develop drug-resistant HIV which can be transmitted to others.
- A physical buffer-stock of HIV program commodities is maintained at the central warehouse to ensure uninterrupted supply to facilities. The buffer stock is maintained to cover to **6 months** consumption.
- **Responsibilities:**
    - All health workers: support supply management by filling the standard MOH forms, patient cards, registers and reporting forms.
    - Officer in-charge of pharmacy: manage and account for all commodities received.
    - District Health Management Teams: coordinate and supervise.
- A dedicated HIV Program Logistics Team (**HIV Logistics**) working under MOH Depts. for Health Technical Support Services and for HIV and AIDS actively coordinates procurement, supply planning and distribution of medicines and lab supplies for the HIV and STI Programs.
- Contact HIV Logistics by email (**hivdeptlogistics@gmail.com**) or call **toll-free** on working days 7:30 – 16:30:
    - **5 91 91** (from Airtel phone)
    - **68 82** (from TNM phone)
- Ask HIV Logistics for help and get an **authorization code before** any of the following transactions with ARVs and HIV test kits:
    - Getting additional supplies from warehouse.
    - Moving stocks from / to another facility.
    - Disposing expired / spoiled stocks.
- **Notify** HIV Logistics about (even if suspected):
    - Damaged or inappropriate stocks received.
    - Serious (suspected) side effects.

24.1 HIV commodity supply cycle

- Table 23 shows the different commodity groups currently managed by the HIV Program.

Table 23: Drugs and testing supplies managed by the HIV Program

Commodity group	Examples	Supply*
ARVs	(All ARVs, incl. PEP and infant prophylaxis)	**E**
OI	Cotrimoxazole for CPT	**E**
	Isoniazid + pyridoxine for IPT	**E**
	Cotrimoxazole, other antibiotics, fluconazole, chemotherapy	**S**
STI	Standard / alternative antibiotics, acyclovir, clotrimazole	**S**
PIFP	Condoms, Depo-Provera	**S**
Analgesic	Morphine, codeine	**S**
DBS kits	for EID and VL samples	**E**
Tests	HIV and syphilis rapid test kits	**E**

Supply*: **E** = item managed exclusively through HIV Program. **S** = items supplemented by HIV Program in addition to essential medicine supplies.

- HIV commodities are delivered every 2 months from a central warehouse (Lilongwe) directly to all facilities.
- Distribution lists for all facilities are calculated based on the patient and stock reports collected during quarterly HIV Program supervision and reported through the Logistics Management Information System.
- Actively support the **2-monthly supply cycle** and the **ongoing management** following the 11 steps in **Figure 8**.

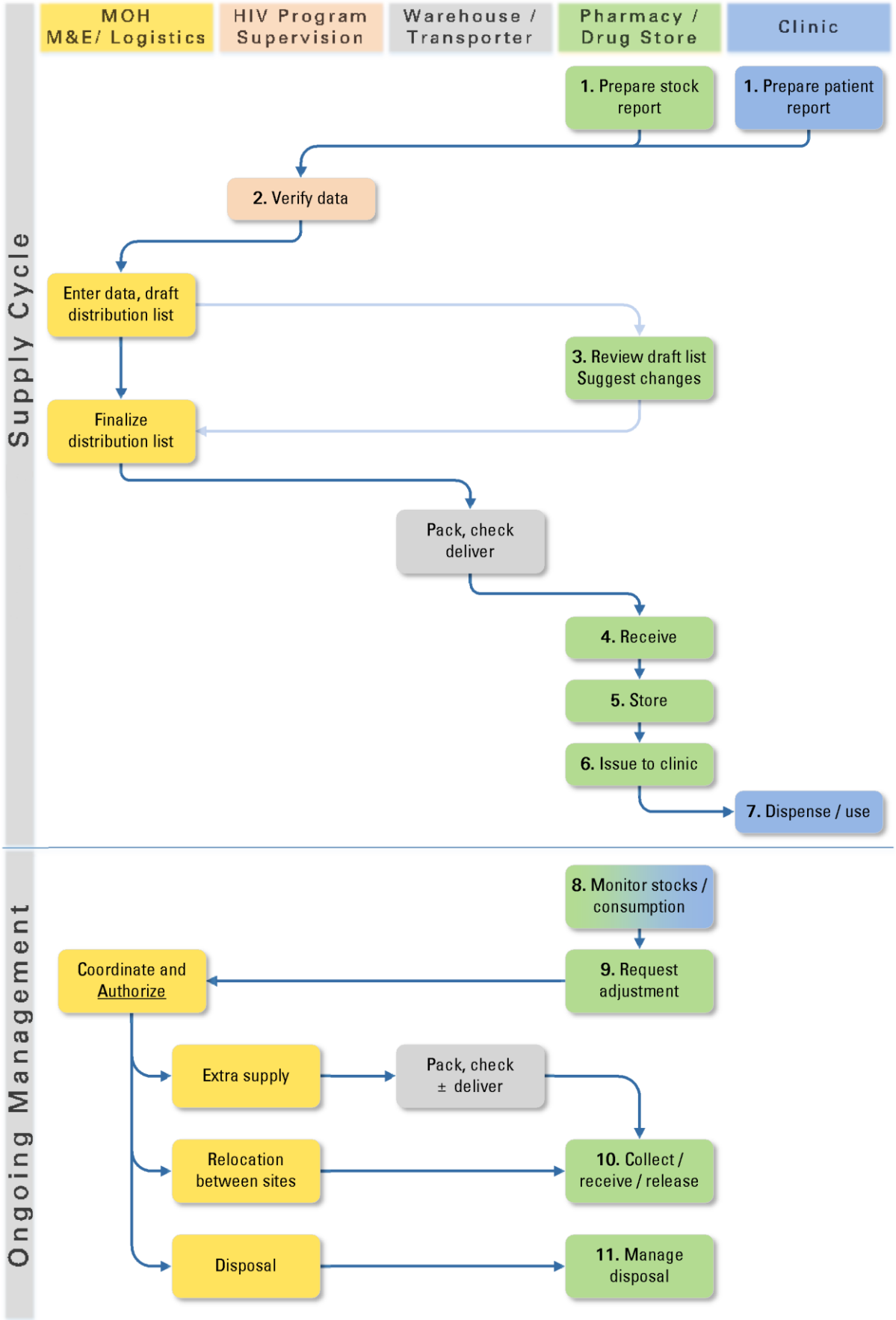
1. Prepare stock / patient report

- Confirm each commodity is sorted by expiry date.
- Do physical count of stock on hand (SOH). Exclude any units that may have already expired.
- Ensure all available stock is counted, including in bulk store, at the clinic / HIV testing rooms, etc.

2. Verify data

- Ensure all storage areas and patient records / registers are accessible on the day of supervision.
- The HIV Program supervision team will work with facility staff to verify:
    - Stock reports by doing a physical count.
    - Patient report by reviewing patient cards and registers.
- Check that the stock report filled during supervision is complete and accurate. The supervision team and the In-Charge of pharmacy are responsible for confirming this by signing the form.

Figure 8: Flowchart for HIV commodity supply management



3. Review draft distribution list

- **2-monthly consignments** are calculated by *HIV Logistics* from patient numbers and stock reports collected at the last supervision visit.
    - All ARVs and HIV test kits included should be about **2 MOS** (months of stock, see below).
    - Consignments are scheduled to arrive in every 2 months.
    - Facilities should have about **2 MOS** remaining when the new consignment arrives (site-level buffer). This should bring the total to about **4 MOS**.
- HIV Logistics will circulate the *draft distribution list* to anyone registered with their email address. To register, send an email request to hivdeptlogistics@gmail.com. Anyone can also subscribe for an automatic notification by email and/or SMS whenever a distribution list is posted for review on the HIV Dept. website (www.hiv.health.gov.mw).
- Review and confirm that the items and quantities are correct and adequate for you. Submit any suggested changes (by email, SMS or phone) before the deadline shown on the draft list.

4. Receive consignment

- Inspect the entire consignment in the presence of a witness designated by DHMT/ facility In-Charge:
    - Physically count all re-packed / loose units. Originally sealed boxes do not need to be opened for counting of units. Add up total units received for each item.
    - Check expiry date for all items.
    - Write physical count for each item into the respective box on the *delivery note*. Write 0 (zero) for any items not received – don't leave any boxes empty.
- Sign, date and stamp the *delivery note* to confirm receipt of the items as indicated.
- The person signing on the delivery note is accountable for all items s/he has signed for. The In-Charge of pharmacy / facility will be held responsible for any discrepancies noted later.

5. Store

- Immediately move all items received to a secure storage area (clean, dry, cool and off the floor).
- Enter quantity and date of receipts on *stock cards* without delay.
- Arrange items by expiry date to make it easy to follow the *First Expiry -First Out* principle (*FEFO*).

6. Issue to clinic

- Fill *Requisition and Issue Vouchers* for all commodity requests from the clinic.
- Always follow the *FEFO* principle.
- Immediately update *stock card* when moving items out of the pharmacy.
- Limit the amount of stock stored at the clinic to 1 week consumption.

7. Dispense / use

- Ensure that the patient has fully understood:

- How and when to take their drugs.
- Possible side-effects; which side-effects require coming to the health facility.

- Account for all HIV commodities dispensed. Specify type and quantity:
  - On *patient master cards* (ART, Exposed child)
  - *Dispensing registers* for special drugs (Diflucan)
  - *Daily Activity Registers (DAR)* for HIV test kits.

- The *DAR* is used for tracking use of HIV test kits.
  - Keep a separate register at all places where HIV testing is done.
  - Use separate pages for the different types of tests (Determine, Uni-Gold).
  - Test kits *used for clients* must match entries in the HIV testing Register.
  - The DAR includes sets of 3 carbonated sheets: keep white sheet at facility; send blue sheet to DHO; retain pink/yellow sheet for collection by HIV Logistics (MOH).
  - Fill monthly summary on HIV testing report by adding numbers from all DAR used at the facility.

8. Monitor stocks / consumption

- Do a **physical stock count** for all items (in store and at the clinic) and update stock cards:
  - On the last working day of each month.
  - When handing over pharmacy management to another staff member.
  - Whenever discrepancies are noted.

- **Calculate** average monthly consumption (**AMC**) and months of stock (**MOS**) for all ARVs and HIV test kits after doing the monthly physical count:

$$\textbf{AMC} = \frac{\text{units used in last 3 months}}{3} \qquad \textbf{MOS} = \frac{\text{stock on hand}}{\text{AMC}}$$

- Be alert: commodity shortages can be anticipated before they happen:
  - Large number of transfers in.
  - Patients moving to 2nd line or alternative regimens.
  - Rapid growth through new initiations.

- As soon as commodity **shortage** is **suspected or noticed**:
  - Contact *HIV Logistics* for additional supply (see below).
  - Inform all relevant staff members.
  - Prioritize use (e.g. HIV test kits for sick patients needing to start ART, women at ANC and maternity, etc.).
  - Shorten supply interval (e.g. give ARVs for 1 month instead of 3).

- Commodity **excess:** more than **4 MOS**, especially if units will expire before they can be used:
  - Contact *HIV Logistics* for to request stock relocation (see below).

9. Request adjustment

- Call *HIV Logistics* as soon as possible if **shortage**, **excess** or **expiry** is noted.
- Before calling, prepare the following information:
    - Number of tins / bottles / tests remaining.
    - Expiry date
    - Number of patients on this regimen / approximate AMC.
    - When additional stocks are needed / to be sent to other site.
    - If own transport can be organized.
- *HIV Logistics* will:
    - Review the information and find out the reason for the problem.
    - Coordinate: **extra allocation from the warehouse**, **relocation of stocks between sites**, or register **disposal of expired commodities**.
    - Send a unique ***Authorization Code*** for each item by SMS or phone.
- Confirm receipt of authorization codes by sending 'OK' by SMS or by calling *HIV Logistics*.
- Fill a ***Registration Form for Relocation or Disposal of HIV Commodities*** for each adjustment.
    - Write the authorization code for each item on the form.
    - Keep Registration Forms in the pharmacy to account for all commodity transactions.
- Never relocate or dispose HIV commodities without *authorization code*. In exceptional circumstances (threating stock-out and no phone coverage / no answer), stocks may be relocated and notification and *authorization codes* must be obtained at the earliest opportunity.

10. Collect / receive / release stock (from adjustment)

- When collecting extra consignments from the warehouse:
    - Ask for the size of the consignment and make sure it can be safely transported (security, sun/rain protection, etc.). Partial collection will not be allowed.
    - Make specific appointment and get directions from *HIV Logistics*.
    - Bring ID (passport, driving license, etc.) and official facility stamp.
    - Inspect the whole consignment. The collecting officer and a witness must fill, sign and stamp the delivery note as usual.
    - There is no need to fill a *Registration Form for Relocation* for extra allocations from the warehouse.
- Relocating stocks between facilities:
    - Fill a *Registration Form for Relocation* and write the *authorization code* for each item.
    - Keep the white copy of the form at the facility releasing the stock. This is mandatory to account for commodities given away to another site.
    - Give the pink copy to the facility receiving the relocated commodities.

11. Manage disposal

- Separate expired commodities from usable stock as soon as possible.
- Notify HIV Logistics, get ***Authorization Code*** and fill ***Registration Form for Disposal***
- Contact the District Pharmacist and arrange for transfer of expired items for controlled destruction.

25 Appendix

Figure 9: Body surface area estimation for calculation of paclitaxel dose

BSA	Height in cm																									
Weight in kg	140	142	144	146	148	150	152	154	156	158	160	162	164	166	168	170	172	174	176	178	180	182	184	186	188	190
36	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.4	1.4	1.4	1.4
38	1.2	1.2	1.2	1.2	1.2	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4
40	1.2	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.5
42	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.5	1.5	1.5	1.5	1.5
44	1.3	1.3	1.3	1.3	1.3	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
46	1.3	1.3	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.6
48	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.6	1.6	1.6	1.6	1.6
50	1.4	1.4	1.4	1.4	1.4	1.4	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6
52	1.4	1.4	1.4	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.7
54	1.4	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.7	1.7	1.7	1.7	1.7
56	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
58	1.5	1.5	1.5	1.5	1.5	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
60	1.5	1.5	1.5	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.8	1.8
62	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.8	1.8	1.8	1.8	1.8
64	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8
66	1.6	1.6	1.6	1.6	1.6	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9	1.9
68	1.6	1.6	1.6	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9	1.9	1.9	1.9	1.9
70	1.6	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9	1.9	1.9	1.9	1.9	1.9	1.9
72	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1.9
74	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1.9	2.0	2.0	2.0
76	1.7	1.7	1.7	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1.9	2.0	2.0	2.0	2.0	2.0
78	1.7	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1.9	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
80	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1.9	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.1
82	1.8	1.8	1.8	1.8	1.8	1.8	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1.9	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.1	2.1	2.1
84	1.8	1.8	1.8	1.8	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1.9	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.1	2.1	2.1	2.1	2.1
86	1.8	1.8	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1.9	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.1
88	1.8	1.9	1.9	1.9	1.9	1.9	1.9	1.9	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.2
90	1.9	1.9	1.9	1.9	1.9	1.9	1.9	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.2	2.2	2.2
92	1.9	1.9	1.9	1.9	1.9	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.2	2.2	2.2	2.2	2.2
94	1.9	1.9	1.9	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.2	2.2	2.2	2.2	2.2	2.2	2.2
96	1.9	1.9	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.3
98	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.3	2.3	2.3
100	2.0	2.0	2.0	2.0	2.0	2.0	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.3	2.3	2.3	2.3
102	2.0	2.0	2.0	2.0	2.0	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.3	2.3	2.3	2.3	2.3	2.3
104	2.0	2.0	2.0	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.3
106	2.0	2.0	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.4	2.4
108	2.0	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.4	2.4	2.4
110	2.1	2.1	2.1	2.1	2.1	2.1	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.4	2.4	2.4	2.4	2.4
112	2.1	2.1	2.1	2.1	2.1	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.4	2.4	2.4	2.4	2.4	2.4	2.4
114	2.1	2.1	2.1	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.5
116	2.1	2.1	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.5	2.5
118	2.1	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.5	2.5	2.5	2.5
120	2.2	2.2	2.2	2.2	2.2	2.2	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.5	2.5	2.5	2.5	2.5

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