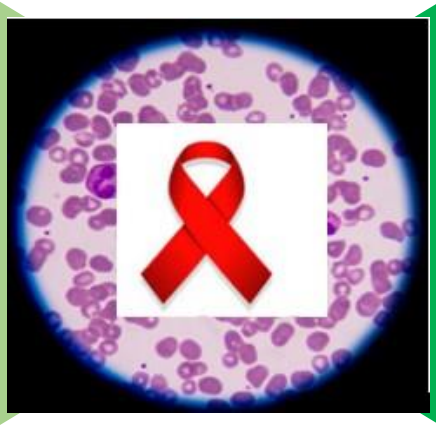
FEDERAL REPUBLIC OF NIGERIA
FEDERAL MINISTRY OF HEALTH
Department of Public Health

NATIONAL GUIDELINES FOR THE MANAGEMENT OF TB/HIV CO-INFECTION IN NIGERIA



National Tuberculosis, Leprosy & Buruli Ulcer Control Programme
&
National AIDS & STIs Control Programme

January 2021, Third Edition

Foreword

TB and HIV constitute major public health problems in Nigeria. The burden of these diseases is further compounded by the impact they have on each other; HIV fuels the burden of TB while TB on the other hand is the commonest infection among People Living with HIV (PLHIV). The interaction between these two diseases increases the morbidity and mortality among TB/HIV co-infected patients and also stretches the already challenged infrastructure of the health sector.

Nigeria is among the 14 countries that are on the three high burden country lists for TB, TB/HIV and Multi-drug resistant TB. The TB burden in the country is further compounded by the high HIV prevalence of 1.4% (National AIDS Indicator and Impact Survey NAIIS, 2018). The Federal Ministry of Health in its effort at providing effective and coordinated response to the dual epidemics of TB and HIV established the National TB/HIV Working Group in 2006.

The Ministry has recorded significant progress since commencement of TB/HIV collaborative activities in the country; the proportion of registered TB patients with documented HIV status increased from 10% in 2006 to 97% in 2019 with a current co-infection rate of 11% (NTBLCP Annual Report 2019). The proportions of TB/HIV co-infected patients accessing Cotrimoxazole Preventive Therapy (CPT), Antiretroviral therapy (ART) and other HIV support services have also increased. Implementation of the 3Is (Intensify TB case Finding, Isoniazid Preventive Therapy and TB Infection Control) has also recorded progress though suboptimal

The third edition of the Guidelines for Management of TB/HIV co - infection in Nigeria was therefore reviewed to support efforts at country level in scaling up implementation of TB/HIV collaborative activities taking into consideration lessons learnt on the field in the previous years and other global advancement. The guideline will enhance the capacities of health workers in the management of TB/HIV co-infected clients and is therefore an essential document for all stakeholders providing support for TB/HIV collaborative activities at all levels.

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Acknowledgement

The National Guidelines for Management of TB/HIV co- infection is a vital tool that aims at providing appropriate guidance for management of individuals infected with the two diseases.

I wish to express my appreciation to members of the technical team, who have contributed to the review of this document. We are grateful to World Health Organization (WHO), the Donor Agencies, TB/HIV stakeholders and Implementing Partners for their support.

Our special appreciation goes to the Clinton Access Initiative (CHAI) who supported financially the process of reviewing this guideline with the UNITAID funding

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Executive summary

The 2021 National Guidelines for the management of TB/HIV co – infection in Nigeria is a seven-chapter document that provides general and specific guidance on the management of TB/HIV co – infection as it relates to preventive strategies, diagnosis and treatment modalities in adults, adolescents and children. It highlights the essential package of care and services required as well as mechanisms for effective co – ordination between the two disease entities for a seamless delivery of care.

The first chapter introduces the guidelines in general, the epidemiology of TB/HIV in Nigeria, the target audience, mechanisms for co – ordination of care across all levels of healthcare with specific insights into the constitution of the technical working groups and their terms of reference.

Chapter two provides guidance on the required TB/HIV services at various service delivery points in healthcare settings as well as the community. It lays specific emphasis on integration of TB/HIV services into PMTCT, RMNCAH+N and key populations as well as across diagnostic platforms for multi – disease testing.

Chapter three and four focuses on screening, diagnosis and treatment of both diseases in adults, adolescents and children with special considerations for patients with co – infection. It highlights the overlapping effects associated with the concurrent use of anti – TB medicines and Antiretrovirals with emphasis on Immune reconstitution syndrome and provides guidance on the importance of adherence to medications in co – infected patients.

The fifth chapter focuses on Tuberculosis preventive therapy (TPT); the different regimens, screening, monitoring, management of treatment interruption as well as contact investigation and management. Chapter six is dedicated to the management of other common opportunistic infections and their preventive strategies with special emphasis on Cotrimoxazole Preventive Therapy (CPT)

Finally, the seventh chapter deals with the strategies for infection prevention and control of TB and HIV in healthcare settings.

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List of Acronyms

3TC	Lamivudine
ABC	Abacavir
ADA	Adenosine deaminase assay
AHD	Advanced HIV Disease
AIDS	Acquired Immune Deficiency Syndrome
ART	Anti-Retroviral Therapy
ARV	Anti-Retroviral
AZT	Zidovudine
BU	Buruli Ulcer
CB-DOTS	Community Based-Directly Observed Treatment
CBOs	Community-based organizations
CHWs	Community health workers
COVID-19	Coronavirus disease - 2019
CPT	Cotrimoxazole Preventive Therapy
CSF	Cerebrospinal fluid
CSOs	Civil Society Organisations
DOT	Directly Observed Therapy
DOTS	Directly Observed Treatment - Short course (WHO Strategy)
DR-TB	Drug resistant TB
DS-TB	Drug susceptible TB
DTG	Dolutegravir
EFV	Efavirenz
EPTB	Extra-pulmonary Tuberculosis
FDC	Fixed-Dose Combination
FTC	Emtricitabine
HCV	Hepatitis C virus
HCWs	Health Care Workers
HF	Health Facility
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma virus

IEC	Information, education and Communication
INH	Isoniazid
KP	Key population
LACA	Local Government Action Committee on AIDS
LASCP	Local Government AIDS and STI Control Program
LF-LAM	Lateral flow lipoarabinomannan
LGTBLS	Local Government TB and Leprosy Supervisor
M&E	Monitoring and Evaluation
MDR-TB	Multi-Drug Resistant Tuberculosis
MRI	Magnetic resonance imaging
MTB	Mycobacterium tuberculosis
NACA	National Action Committee on AIDS
NAIIS	National HIV/AIDS indicator and impact survey
NASCP	National AIDS and STI control Program
NGO	Non-Governmental Organization
NTBLCP	National Tuberculosis, Leprosy and Buruli ulcer Control Program
OI	Opportunistic infections
PCR	Polymerase chain reaction
PITC	Provider initiated HIV Testing and counselling
PLHIV	Persons Living with HIV
PM	Program Manager
PMTCT	Prevention of Mother to Child Transmission
PTB	Pulmonary tuberculosis
RIF	Rifampicin
RMNCAH+N	Reproductive, maternal, new-born, child, adolescent health +nutrition
SACA	State Action Committee on AIDS
SASCP	State AIDS and STI Control Program
SOP	Standard operating procedure
STBLCP	State Tuberculosis, Leprosy and Buruli ulcer Control Program
TAF	Tenofovir alafenamide

TB	Tuberculosis
TDF	Tenofovir disoproxil fumarate.
ToR	Terms of Reference
TPT	Tuberculosis Preventive Therapy
TWG	Technical Working Group
UNICEF	United Nations Children Fund
WBC	White blood cell count

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CHAPTER ONE
INTRODUCTION

1.1 Background

Nigeria is ranked 6th among the 30 high burden TB countries in the world and 1st in Africa with an incidence rate of 219/100,000 population. The country is one of the eight that accounted for two-third of the global TB burden and is listed among the 14 countries with the highest burden of TB, TB/HIV and MDR-TB (WHO global TB report, 2020). A total of 120,266 TB cases were notified in 2019 translating into a TB treatment coverage of 27%, with males accounting for 61% (NTBLCP Annual Report, 2019).

Similarly, Nigeria has the second largest burden of HIV in Africa with a prevalence of 1.4%. Women aged 15–49 years are more than twice as likely to be living with HIV as men (1.9% versus 0.9 %). Among children aged 0–14 years, the prevalence is 0.2% (NAIIS report 2018). The HIV prevalence of adolescents in Nigeria is estimated to be 3.5%, the highest among countries in West and Central Africa (UNICEF 2017 report).

HIV is known to increase the burden of TB, while TB is the leading cause of death among People Living with HIV (PLHIV) and was responsible for one-third of the estimated 690,000 deaths from HIV in 2019. Nigeria had an estimated 46,000 incident HIV positive TB cases in 2019 and HIV positive TB mortality rate of 14/100,000 population (WHO global TB Report, 2020). Almost one quarter of the estimated HIV positive incident TB cases remained undiagnosed in 2019 (NTBLCP Annual Report, 2019). These highlight the critical need to improve the diagnosis, treatment and prevention of TB/HIV co-infection in the country. It is imperative that health workers are well informed on the interactions between these two diseases and learn to manage them competently.

1.2 Target Audience

This guideline is targeted at:

- Health care workers providing TB and HIV services at all levels.

- Programme Managers providing mentorship and oversight for both TB and HIV programmes at all levels.
- Policy makers, Partners and other relevant stakeholders.

1.3 Coordinating Care between TB and HIV Care Providers

TB/HIV collaborative activities are coordinated at national, state, LGA and facility levels through the TB/HIV Technical Working Groups (TWGs)/Committees. At the national level, the TWG provides technical guidance to the Ministry of Health in the formulation of policy and implementation of activities for all levels.

1.3.1 Membership and Terms of Reference (ToR) of the TB/HIV coordinating bodies (TWGs/Committees) at all levels

National, State and LGA levels

The recommended membership of the Committee at National, State and LGA levels includes (not restricted to):

- Director of Public Health ``
- National coordinators of TB and HIV programmes
- Representative of State Hospital Management Board
- HIV Programme Managers (NASCP, SASCP, LASCP)
- TB Programme Managers (NTBLCP, STBLCP, LGA TBLS)
- HIV multisectoral response (NACA, SACA, LACA)
- PHCDA (NPHCDA, SPHCDA)
- Representative of all Implementing partners
- DOTS Providers – especially at State and LGA levels
- HIV Service Providers - especially at State and LGA levels
- Ex- TB Patients
- Representative of the TB Network/CSOs in TB
- Representative of the PLHIV Network
- Representative of the HIV Civil society organizations
- Representative of the Academia
- Representative of the Media

- Religious leaders
- Community members

ToR of the working group at National/State/LGA levels

The working groups will support Government at National, State & LGA levels in:

- Promoting collaboration between TB and HIV programmes.
- Developing/Adopting technical framework to guide all stakeholders for better TB control among HIV-infected people and effective HIV prevention and care among TB patients.
- Reviewing and tracking progress of implementation of TB/HIV collaborative activities, identifying challenges and proffering solutions.
- Advocating for increased resources for TB/HIV collaborative activities.
- Promoting Research in TB/HIV control and creating data base on TB/HIV collaborative activities at all levels.
- Joint planning, implementation, monitoring and evaluation of TB/HIV collaborative activities.
- Promoting Public private partnership in TB/HIV collaborative activities
- Promoting continuity of TB/HIV services during emergencies

At Facility level:

The suggested membership of this committee includes:

- Representative of Hospital Management
- Staff from DOTS clinic
- Staff from HIV unit
- Representative from the Laboratory unit
- Representative from Pharmacy department
- Representative of the support groups in the facility
- LGA TBLS
- LGA HIV programme managers
- Representative of record or M&E unit

Note: This coordinating committee can be incorporated into an existing committee in the facility where feasible

ToR of the TB/HIV Committee at facility level

- To review and track progress in the implementation of TB/HIV collaborative activities in the facility.
- To establish/strengthen referral and linkages between TB & HIV services.
- To identify challenges inhibiting effective service delivery and proffers solutions.
- To plan, implement and monitor TB/HIV activities.
- To support facility staff in documentation of all TB/HIV services.
- To support collection, collation, analysis and utilization of TB/HIV data.
- To ensure a proper feedback mechanism to all stakeholders.
- To ensure continuity of TB/HIV services during emergencies.

Key points:

- **All TB/HIV data from both TB and HIV clinics should be reviewed, updated and harmonized during the facility TB/HIV meeting.**
- **The facility TB/HIV Committee should meet at least once every month.**
- **All secondary and tertiary institutions providing TB and HIV services should set up a TB/HIV committee at the facility level to enhance effective integration of TB/HIV services.**

CHAPTER TWO
TB/HIV SERVICES

2.1 Introduction

The goal of TB/HIV collaboration is to reduce illnesses and death among co-infected patients. TB and HIV services are provided at the health facility and community levels. However, referral mechanisms must be ensured between the community and facility.

2.2 TB/HIV Services

The available TB/HIV services include:

- Provider initiated HIV Testing and counseling (PITC) for all presumptive and diagnosed TB cases.
- Anti-retroviral Therapy (ART) for all HIV-positive TB patients.
- Cotrimoxazole Preventive Therapy (CPT) for all HIV positive TB patients to prevent common opportunistic infections.
- Alleviating common conditions associated with HIV.
- TB clinical screening for all PLHIV at every visit.
- Radiological screening (Chest x-ray) for newly diagnosed PLHIV (at point of enrollment).
- Diagnosis for TB among PLHIV with presumptive TB.
- Treatment for TB among PLHIV.
- Preventing TB in PLHIV without active TB using TB Preventive Therapy (TPT).
- TB infection control at all units in the facility and the community.
- Care and support services including treatment Support, community and home-based care.
- Adherence counseling on medicine use.

2.3 Models of delivery of TB/HIV services at facility level

TB/HIV services should be provided in a patient centered manner. The models of delivery in the country include:

1. Full-service integration (One-stop shop model)

- All TB and HIV services are provided by the same healthcare worker under the same roof.
- Strict infection control policy must be in place.

2. Partial service integration
    - ART and DOTS clinic are in different location within the same facility
    - Services are provided by different healthcare workers
    - Healthcare workers must ensure strengthened intra-facility referrals and complete documentation of referral outcomes.
3. Separate service provision
    - Stand-alone DOTS and ART site
    - Stand-alone DOTS offer PITC (for presumptive and diagnosed TB) but refers HIV positive TB patients to ART services in another facility
    - Healthcare workers must ensure strengthened inter-facility referral and complete documentation of referral outcomes.

The preferred approach is the "One-stop shop model", where patients receive all services in the same setting by the same provider.

Irrespective of the model of TB/HIV service delivery used, it is expected that the TB/HIV service will be provided by competent officers in a comprehensive, compassionate, cost effective and patient centered manner.

2.4 Delivery of TB/HIV services at community level

It is important for HCWs and community-based organizations (CBOs) involved in TB and HIV control at the community level to interact more frequently at every available opportunity.

The following activities should be implemented by HCWs in the community:

- Provide patient and family education with the basic facts on TB and HIV including causes, transmission, and on adequate ventilation within the household to prevent TB infection
- Screen all newly diagnosed PLHIV in the community for symptoms of TB to identify presumptive TB cases
- Screen every PLHIV on ART coming in contact with HCWs in the community for any reason for symptoms of TB to identify presumptive TB cases.
- Screen all contacts of bacteriologically positive TB cases, urban slum dwellers and PLHIV for symptoms of TB to identify presumptive TB cases.
- Document all PLHIV identified with presumptive TB in the HIV recording and reporting tools.
- Link the identified presumptive TB with the DOT center for further management
- Support effective adherence for patients on treatment.
- Provide accompanying services (volunteers) and ensure results retrieval where applicable.

2.5 Integration of TB/HIV services into other programmes

There is growing evidence regarding the burden and detrimental effects of TB among women, children, adolescents and key populations, especially among those living with HIV. This highlights the need for integrating TB/HIV activities into the following programmes:

2.5.1 PMTCT and RMNCAH+N services

The following activities are recommended at the PMTCT and RMNCAH+N points

- All pregnant women with HIV should be screened for TB at each visit in line with the National guidelines.
- A pregnant HIV positive woman with presumptive TB should be tested using Xpert MTB/RIF or Truenat MTB-RIF Dx platforms.
- If the woman is diagnosed with TB disease, treat or refer to the nearest DOTS center for anti-TB medicine immediately.

- If active TB disease is ruled out, TPT should be provided in accordance with the National guidelines.
- Screen all infants, children and adolescents for TB or refer appropriately. If screening suggests presumptive TB, manage according to the National guidelines
- If TB is excluded in children and adolescents born to a mother with active TB, commence TPT.
- Neonates born to women of unknown HIV status should be vaccinated as the benefits of BCG vaccination outweigh the risks.
- Neonates with unknown HIV status born to HIV infected women should be vaccinated if they have no clinical evidence suggestive of HIV disease, regardless of whether the mother is receiving ART.
- Neonates with HIV infection confirmed by early virological testing, BCG vaccination should be delayed until ART has been started and the infant confirmed to be immunologically stable (CD4 >25%).
- In HIV-infected children on ART, those clinically and immunologically stable (CD4% >25% for <5 years or CD4 count ≥200 for >5 years) should be vaccinated with BCG.
- Infants born to a mother with HIV infection should receive appropriate ARV prophylaxis.

2.5.2 Key Populations (KPs)

The categories of individuals prioritized as key populations (KPs) include sex workers, people who inject drugs (PWIDs), people who engage in anal sex, people in congregate settings. The following activities are recommended for key populations.

- KP should be screened for TB at every visit or contact with health services to identify presumptive TB cases.
- KP with presumptive TB should be evaluated using Xpert MTB/RIF assay or Truenat MTB-RIF Dx.
- KP diagnosed with TB should be offered or referred for patient centered TB treatment.

- HIV positive KP without active TB should receive TPT using the National guidelines.

2.6 Diagnostic platforms for integration

TB/HIV integrated service delivery should be promoted to ensure provision of a comprehensive package for diagnostic and treatment services to improve patient-centered care. This will enable platforms such as GeneXpert and other PCR machines for TB, HIV, HPV, HCV, COVID-19 and other diseases to be leveraged upon to increase case finding across disease areas.

CHAPTER THREE
Management of TB/HIV Co-infection in Adults

3.1 Introduction

The treatment of active TB (pulmonary or extra-pulmonary) in patients with HIV should follow the general principles guiding treatment for patients without HIV. However, prompt initiation of TB treatment is required in co–infected patients. Close collaboration between TB and HIV programmes is crucial in supporting general health care service providers. Important considerations related to the use of ART in patients with active TB include:

- When to start ART.
- Significant pharmacokinetics drug-drug interactions between anti-TB and ARV agents.
- The additive toxicities associated with concomitant ARV and anti-TB drug use.
- The development of TB-associated immune reconstitution inflammatory syndrome (IRIS) after ART initiation.

3.2 Management of TB in HIV

There is need for all health care workers (HCWs) to have basic knowledge on the management of TB among PLHIV.

3.2.1 Screening of PLHIVs for TB

Diagnosis of TB among PLHIV starts with early identification of PLHIV with presumptive TB. This is done by screening all PLHIV for signs and symptoms of TB at every visit to a health facility or contact with a health worker.

All PLHIV should be asked for the following at every visit:

- History of current cough.
- Fever.
- Weight loss.
- Night sweats.

PLHIV with any of the above listed signs and symptoms should be evaluated further for TB using the algorithm for TB screening among PLHIV as shown in figure 1

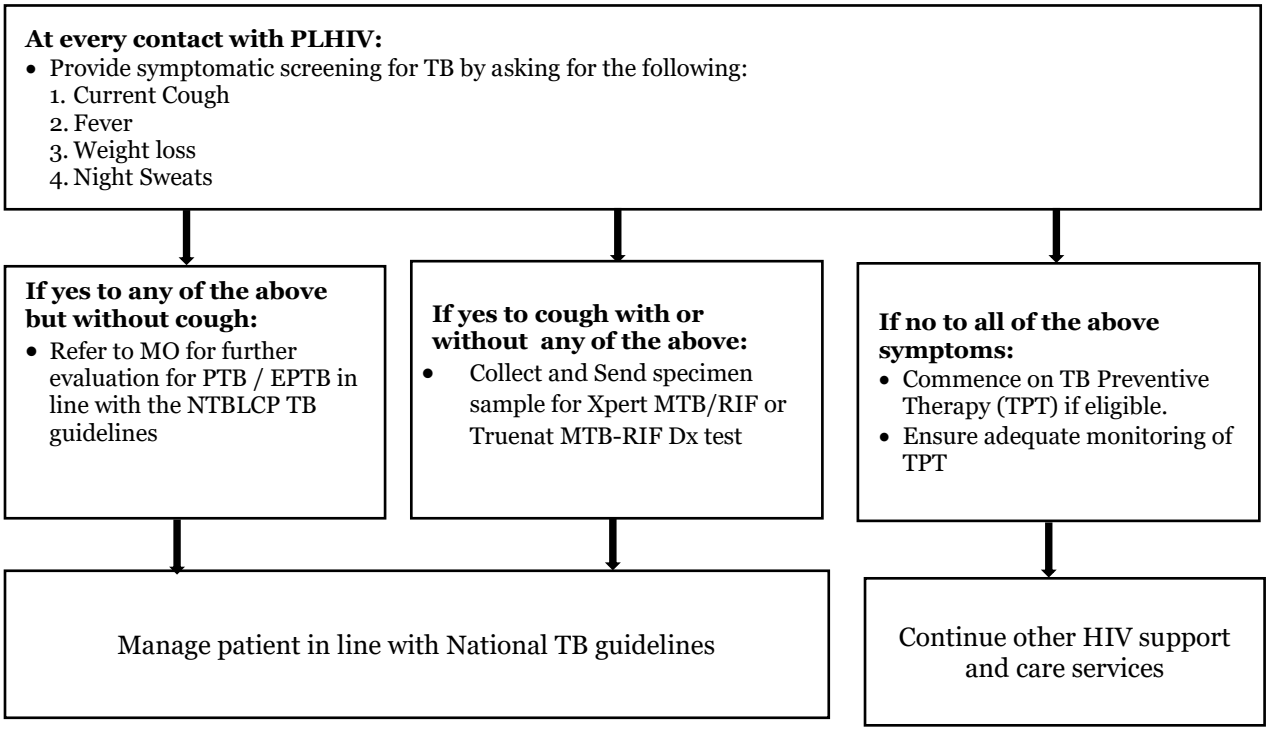


Figure 1 : Algorithm for TB screening among Adult living with HIV

All TB symptomatic PLHIV must be sent for Xpert MTB/RIF or Truenat MTB-RIF Dx test as a priority

3.1.2 Diagnosis of Pulmonary TB (PTB) among HIV Positive Adult Clients

Pulmonary TB (PTB) is still the commonest form of TB among PLHIV. Pulmonary TB is defined as TB limited to the lung parenchyma. The presentation depends on the degree of immunosuppression. The table below shows how the clinical, laboratory and radiological features differ in early and advanced HIV infection.

Table 1: Clinical, laboratory and radiological features of TB in early and advanced HIV infection

Features of PTB	Stage of HIV infection	
	Early disease	**Advanced HIV Disease**
Clinical features	Often resembles post-primary PTB	Often resembles primary PTB
Sputum Xpert MTB/RIF or Truenat MTB-RIF Dx test	Often positive	May be negative
Urine LF-LAM*	Often negative	Often positive
Chest x-ray appearance	Often cavities	Often infiltrates with no cavities

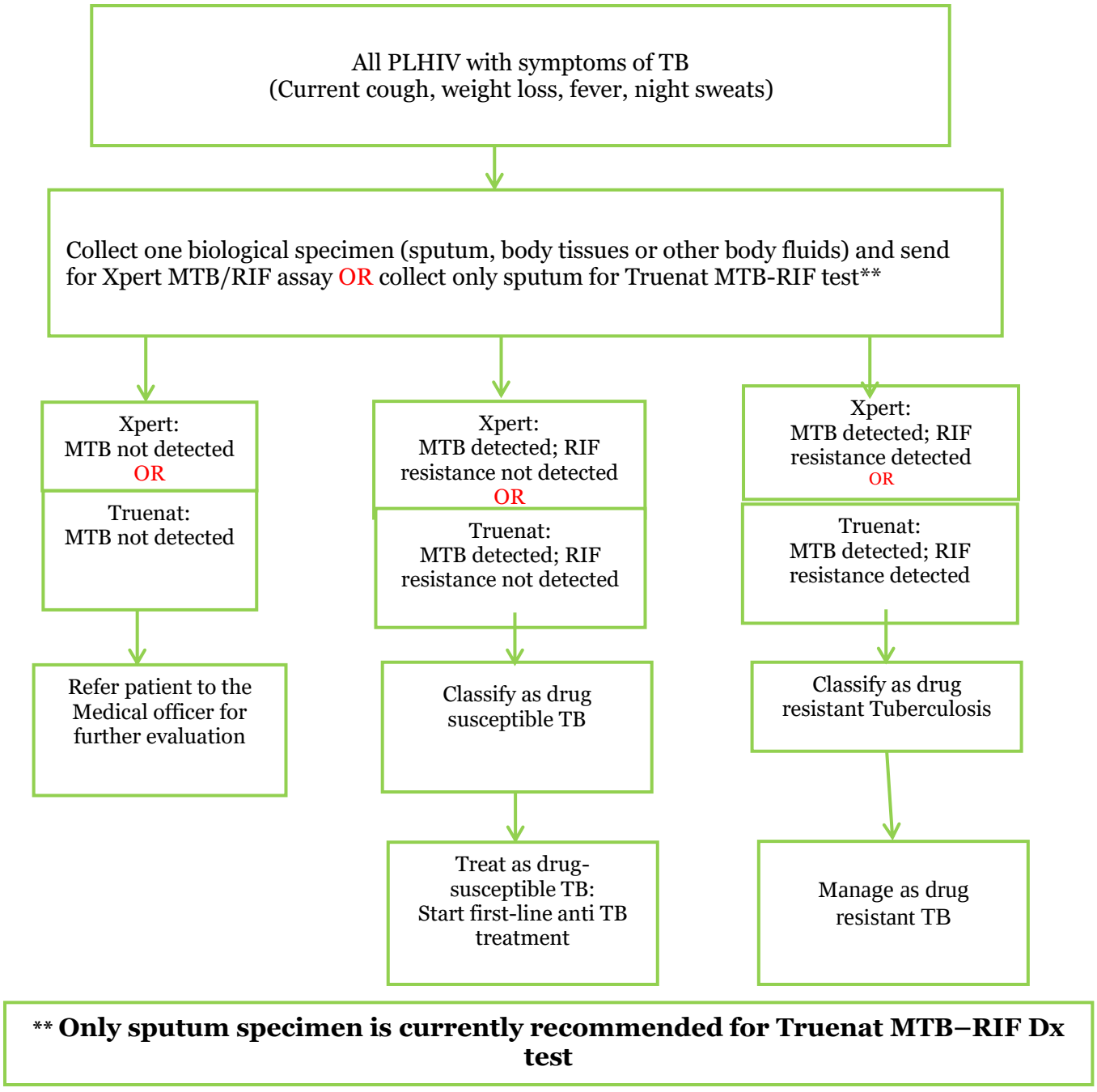
****Urine LF-LAM is only recommended as a screening test for TB in PLHIV with AHD***

The National guideline recommends the use of Xpert MTB/RIF assay as the first line of diagnosis for all presumptive TB cases. All PLHIVs should be tested for TB using Xpert MTB/RIF assay as a matter of priority. When Xpert MTB/RIF test is not available, Truenat MTB-RIF Dx assay may be used.

AFB smear microscopy is not recommended for diagnosis of TB among PLHIV.

Sample collection

One specimen (sputum, cerebrospinal fluids (CSF), pleural fluid, stool, lymph node aspirate and other body fluids) should be collected on the spot and sent to GeneXpert site for testing within 24hours. When Xpert MTB/RIF test is not available, sputum should be collected for Truenat MTB-RIF Dx assay



3.2.3 Diagnosis of Extra Pulmonary TB (EPTB) among PLHIV

The common forms of extrapulmonary TB (EPTB) associated with HIV include: lymphadenitis, pleural effusion, pericardial disease, miliary disease, osteo-articular disease, meningitis. Symptoms or signs due to EPTB depend on the site involved. Regardless of the site of disease, there are usually constitutional symptoms present such

as fever, night sweats and weight loss. The approach for managing common EPTB cases among PLHIV is described in the table below.

Table 2: Approach to diagnosis of common EPTB

Disease Site	Typical clinical presentation	Investigation
TB adenitis	• Asymmetrical, painless, non-tender lymph node enlargement for more than one month • +/- discharging sinus • Most commonly in neck area.	• Xpert MTB/RIF assay, culture and cytology using fine needle aspiration or excisional biopsy when possible. • Chest X-ray. If axillary node enlargement is on same side with site of BCG vaccine administration, consider BCG disease (for children) and refer or manage as applicable.
Pleural TB	• Signs of respiratory distress • Reduced breath sound and chest movement on affected side • Dullness on percussion on affected side • +/-chest pain • Pleural friction rub on affected side • Signs and symptoms are related to the amount of fluid in the pleural space.	• Chest X-ray • Pleural fluid analysis (Xpert MTB/RIF assay, culture, protein content, white blood cell (WBC) count, cytology, adenosine deaminase assay (ADA) • If pleural tap yields pus, consider empyema and refer or manage as appropriate.
TB meningitis	• Headache • Irritability/abnormal behaviour • Vomiting (without diarrhoea)	Cerebrospinal fluid (CSF) analysis (from lumbar puncture): • Gross findings: CSF may look clear, occasionally cloudy or may form spider web if left for a few hours. • Xpert MTB/RIF assay

	• Lethargy/reduced level of consciousness • Neck stiffness • High-pitched cry in under-5 children • Photophobia (aversion to light) • Bulging fontanelle in children <2 years • Signs and symptoms of cranial nerve palsies (e.g. diplopia, squint) • Focal neurological deficits (deafness, blindness, weakness of the limbs) • Convulsions. • Paraplegia (spastic or flaccid paralysis) • Loss of consciousness.	• Microscopy: The WBC count is usually < 500/mm^3 with lymphocyte predominance • Culture • Chemistry: High protein and low glucose levels • CT scan and MRI may show features of intra-cranial collections and Tuberculoma. • Chest X-ray.
Miliary (Disseminated) TB	• Features depend on the site/organ affected but may be usually non-specific. • Lethargy • Fever • Wasting • Failure to thrive in children.	• Chest X-ray • CT scan and MRI may show features specific to lesions in the site/organ affected. • Collect any available specimen depending on site/organ affected and send for investigations as appropriate.
Abdominal TB	• Abdominal swelling with or without ascites • Palpable masses • Diarrhoea • Malabsorption • Cachexia (severe weight loss)	• Abdominal US • Ascitic fluid analysis - Xpert MTB/RIF assay - Culture - Cytology - Chemistry • Biopsy (peritoneal, lymph node, liver etc)

	• Fever • Night sweat.	- Xpert MTB/RIF assay - Histology • CT scan, MRI • Chest X-ray.
Spinal TB	• Deformity of spine e.g., Gibbus (hunch back) • Lower limb weakness/paralysis • Urinary and/or stool incontinence • Paraesthesia (tingling sensations) • Loss of skin sensations (pain and touch).	• X-ray of the spine. • MRI • CT scan.
Pericardial TB	• Signs and symptoms of cardiac failure • Apex beat difficult to palpate. • Distant heart sounds • Pericardial friction rub.	• CXR • Echocardiography • ECG • Pericardial fluid analysis (Xpert MTB/RIF assay, culture, protein content, WBC count and cytology).
TB of long bones and joints	• Swelling of long bones and/or joints with or without limitation of movement • Unilateral effusion (usually knee or hip) • Dactylitis (swelling of the bones of hands and feet) in children. • Discharging sinuses especially when osteomyelitis is present.	• X-ray of the corresponding bone/joint • Joint fluid analysis (Xpert MTB/RIF assay, culture, protein content, WBC count and cytology) • Analysis of any discharge from sinuses (Xpert MTB/RIF assay, culture, protein content, WBC count and cytology).

3.2.4 Classification of TB among PLHIV – Case definitions

A TB patient is an individual who has been diagnosed to have active TB, which can be broadly classified into; bacteriologically confirmed TB or clinically diagnosed TB.

- **A bacteriologically confirmed TB case** is a TB patient with a positive Xpert MTB/RIF assay, Truenat MTB-RIF Dx assay, LF-LAM, smear microscopy or culture result. All such cases should be notified regardless of whether TB treatment has been started.
- **A clinically diagnosed TB case**: is one who does not fulfil the criteria to be considered bacteriologically diagnosed but has been diagnosed with active TB by a health care worker (clinician or other medical practitioners) who has decided to treat the patient with a full course of TB treatment. This includes:
    - Diagnosed based on X-ray abnormalities that are consistent with active TB.
    - Histological and clinical picture suggestive of PTB or EPTB without a laboratory confirmation.
    - Histological and biochemical tests suggestive of TB.

PLHIV with bacteriologically confirmed or clinically diagnosed TB are also classified according to:

- Anatomical site of disease.
- History of previous treatment.
- Drug resistance.

Classification based on Anatomical site of disease

- Defining the site is important for assigning the correct treatment regimen, recording and reporting purposes and to identify the more infectious patients.
- The anatomical classifications of TB are;
    - Pulmonary TB (PTB).
    - Extra-Pulmonary TB (EPTB).

Patients with features of both pulmonary and extrapulmonary TB should be classified as pulmonary TB (miliary TB).

Classification based on History of previous treatment

- TB cases can also be classified according to whether a patient has previously received TB treatment. It is important to identify previously treated patients because they are at increased risk of having drug-resistant TB. This classification includes:

1. New patients.
2. Previously treated patients:
    a. Relapse patients.
    b. Treatment after failure patients.
    c. Treatment after loss to follow-up patients.
    d. Other previously treated patients.
3. Transfer in patients.

Classification based on drug resistance

Cases are classified in categories based on drug susceptibility testing (DST) of clinical isolates confirmed to be M. tuberculosis:

- Monoresistance.
- Polyresistance.
- Multi-drug resistance.
- Pre-extensive drug resistance.
- Extensive drug resistance.
- Rifampicin resistance.

3.2.5 Treatment of TB among adult PLHIV

The treatment of TB in PLHIV is the same as that of the TB patients without HIV infection and the aim is to:

- Cure the patient and restore quality of life and productivity.
- Prevent complications or death.
- Prevent relapse or recurrent disease.
- Reduce transmission of TB to others.
- Prevent the development and transmission of drug resistance.

- Achieve all these with minimal toxicity.

Standard treatment protocols for treating adult PLHIV with drug-susceptible TB.

There are two standard treatment regimens for treating PLHIV diagnosed with TB. These regimens include the following:

1. Regimen 1: **2(RHZE)/4(RH) -** Standard six-month treatment regimen (intensive phase of 2 months and continuation phase of 4 months) for all forms of TB (PTB and EPTB cases – both new and previously treated) **except** for TB meningitis (TBM) and osteoarticular TB cases. Refer to Table 3 below:

Table 3: Regimen and dosages for Adult with susceptible PTB/EPTB cases*

Regimen	**Pre-treatment weight**			
	>25-37 kg	**38-54 kg**	**55-70 kg**	**> 70 kg**
Intensive phase (2 months): • *Combined tablet of RHZE (150mg+75mg+400mg+ 275mg)*	2	3	4	5
Continuation phase (4 months): • *Combined tablet of RH* (150mg + 75mg)	2	3	4	5

**Refers to all PTB and EPTB cases except for TBM & TB of bones/joints*

2. Regimen 2: **2(RHZE)/10(RH) -** Standard twelve-month treatment regimen (intensive phase of 2 months and continuation phase of 10 months) for all cases of TBM and osteoarticular TB cases. Refer to Table 4 below:

Table 4 : Regimen and dosages for adults with TB meningitis and Osteo-articular TB.

Regimen	Pre-treatment weight			
	>25-37 kg	**38-54 kg**	**55-70 kg**	**> 70 kg**
Intensive phase (2 months): • Combined tablet of RHZE (150mg+75mg+400mg+275mg)	2	3	4	5
Continuation phase (10 months): • Combined tablet of RH (150mg + 75mg)	2	3	4	5

Streptomycin is no longer used for first line treatment of TB

Treatment of Drug Resistant TB in PLHIV (DR-TB/HIV)

- The treatment of DR-TB in PLHIV is similar to that in patients without HIV, but the following should be noted:
    - ART plays a crucial role, as mortality in DR-TB/HIV patients without the use of ART is extremely high.
    - Adverse effects are more common in patients with HIV infection. Overlapping toxicities exist with both 2nd line anti-TB treatment and ART.
    - The multiple drugs involved in the management of DR-TB and HIV infection increases the pill burden and the risk of sub-optimal adherence to medications.
    - All DR-TB patients irrespective of CD4+ cell count or viral load count should be put on CPT for the whole duration of DR-TB treatment.
    - Bedaquiline and Efavirenz should not be used together for the management of DR-TB.

Refer to the National DR-TB guidelines for recommendations on the management of clients.

3.2.6 Adjunctive treatment use during TB treatment

Pyridoxine (Vitamin B6): this is recommended for all PLHIV with TB started on TB treatment to prevent peripheral neuropathy mostly caused by INH. The dose of pyridoxine is 50mg daily. In a case where a patient has INH-induced peripheral neuropathy, the dose of Pyridoxine can be administered up to a maximum of 200mg daily, and subsequently reduced to 50mg daily when the symptom subsides.

Steroids (corticosteroids): The use of corticosteroids is recommended in EPTB. High dose steroid treatment for 2-4 weeks and then taper off gradually over several weeks depending on clinical progress is recommended. The response to treatment is assessed clinically. Note the following:

- The use of steroids (corticosteroids), in conjunction with anti-TB drugs, reduce the risk of death in TB meningitis and TB pericarditis.
- Patients with TB meningitis or TB pericarditis should be given corticosteroids.
- Either prednisolone (60mg for adults for an initial period of 21 days followed by tapering off by 25% per week over four weeks) or dexamethasone (0.2–0.4mg/kg/day for a period of 21 days tapering in the same way as above) may be used.

Indication for the use of steroid in PLHIV with TB

- TB meningitis (decreased consciousness, neurological defects or spinal block).
- TB pericarditis (with effusion or constriction).
- TB pleural effusion (when large with severe symptoms).
- TB of adrenal glands (hypoadrenalism).
- TB laryngitis (with life-threatening airway obstruction).
- Severe hypersensitivity reactions to anti-TB drugs
- Renal tract TB (to prevent scarring).
- Massive lymph node enlargement with pressure effects.
- IRIS.

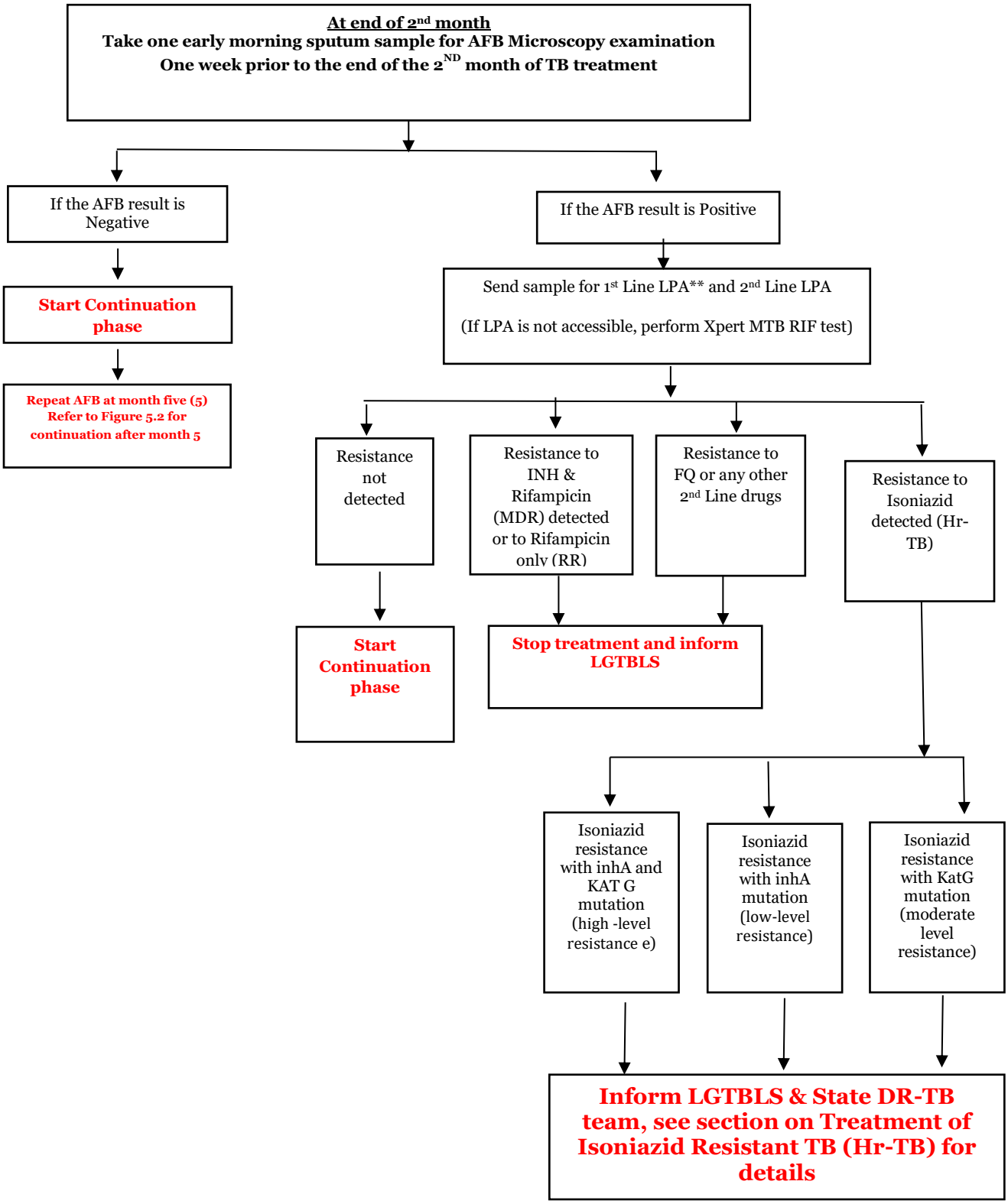
3.2.7 Monitoring TB treatment among PLHIV

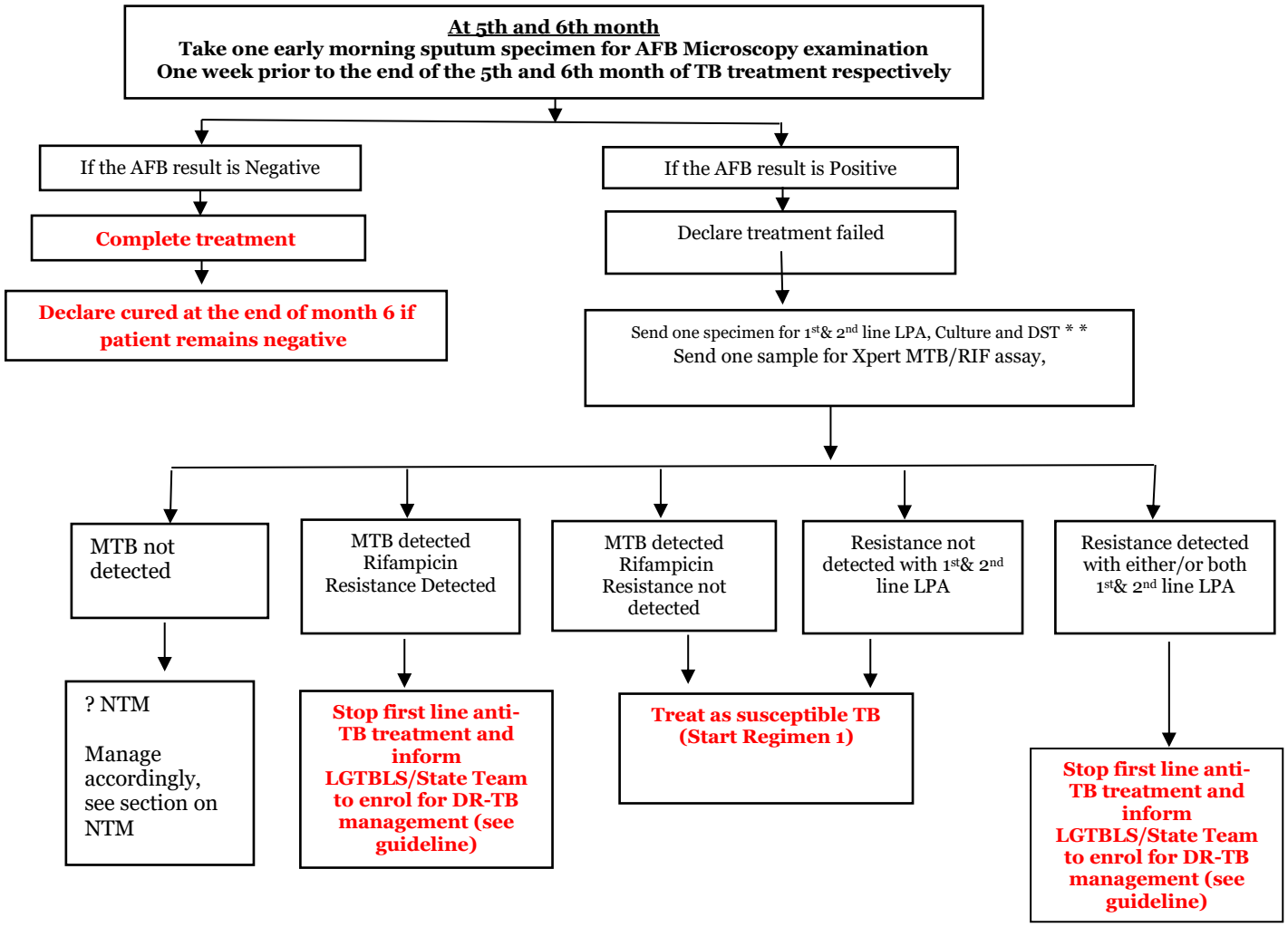
Monitoring progress of tuberculosis patients while on treatment is an essential part of case management. Monitoring is done through the following methods:

a) **Clinical assessment:** This involves regular clinical assessment including weight assessment.

b) **Drug intake:** This is done through assessment of patient's records for regularity.

c) **Sputum AFB smear microscopy:** It involves looking for AFB in sputum specimen at specified intervals: All PLHIV diagnosed with bacteriologically positive TB must be followed up using smear microscopy. One sputum smear examination taken as early morning sample is done at different points during treatment (refer to the flow chart below).


At end of 2nd month
Take one early morning sputum sample for AFB Microscopy examination
One week prior to the end of the 2ND month of TB treatment
If the AFB result is Negative
Start Continuation phase
Repeat AFB at month five (5)
Refer to Figure 5.2 for continuation after month 5
If the AFB result is Positive
Send sample for 1st Line LPA** and 2nd Line LPA
(If LPA is not accessible, perform Xpert MTB RIF test)
Resistance not detected
Resistance to INH & Rifampicin (MDR) detected or to Rifampicin only (RR)
Resistance to FQ or any other 2nd Line drugs
Resistance to Isoniazid detected (Hr-TB)
Start Continuation phase
Stop treatment and inform LGTBLS
Isoniazid resistance with inhA and KAT G mutation (high -level resistance e)
Isoniazid resistance with inhA mutation (low-level resistance)
Isoniazid resistance with KatG mutation (moderate level resistance)
Inform LGTBLS & State DR-TB team, see section on Treatment of Isoniazid Resistant TB (Hr-TB) for details



***** One of the samples must be sent for 1st and 2nd line LPA, Culture and DST and health worker should ensure that the result is available within 5 days for decision making.***

Figure 3 . Algorithm for monitoring using sputum AFB smear microscopy

3.2.8 TB Treatment interruption

Adherence to TB treatment is essential for cure and prevention of drug resistant TB (DR-TB). If a TB patient misses a scheduled appointment or drug collection for a maximum of three days, efforts should be made by HCW to track the patient back to care.

Table 5 below shows the recommended approach to management of treatment interruption

Table 5: Management of TB treatment interruption

Length of interruption	Do Xpert MTB/RIF* or Truenat MTB-RIF Dx	Result of Xpert MTB/RIF or Truenat MTB-RIF Dx	Length of treatment	Action to be taken
< 1 month	No	-	-	Continue treatment and prolong to compensate for missed doses
1 - 2 months	Yes:	MTB not detected	Any length of treatment	Continue treatment and prolong to compensate for missed doses
	Collect and send sample for Xpert MTB/RIF assay or Truenat MTB-RIF Dx	MTB detected RIF resistance not detected		If EPTB, continue treatment and prolong for missed doses.
		MTB detected RIF resistance detected	Any length of treatment	Manage for DRTB. Inform State TB programme and LGA TB Supervisor
2 or more months	Yes Send one sample for Xpert MTB/RIF assay or Truenat MTB-RIF Dx	MTB not detected	One month or more	Clinical decision on individual basis whether to restart or continue treatment
				If EPTB, continue treatment and compensate for missed doses.
		MTB detected	One month or more	Declare as return after loss to follow-up Manage according to Xpert MTB/RIF assay.

*** Xpert MTB/RIF assay can be performed on other specimens such as stool, gastric washing, pleural/pericardial/ascitic fluids, CSF and other body tissues while Truenat can be used for only sputum sample. Refer to NTBLCP SOP on use of Xpert MTB/RIF assay for EPTB specimens.**

3.2.9 TB treatment outcome

The possible TB treatment outcomes are listed below:

- Cured.
- Treatment completed.

- Treatment Failure.
- Died.
- Lost to follow-up.
- Not evaluated.

3.3 Management of HIV among Presumptive and Diagnosed TB Cases

It is recommended that all presumptive and diagnosed TB cases be offered HIV testing services (HTS). Refer to the algorithm below:

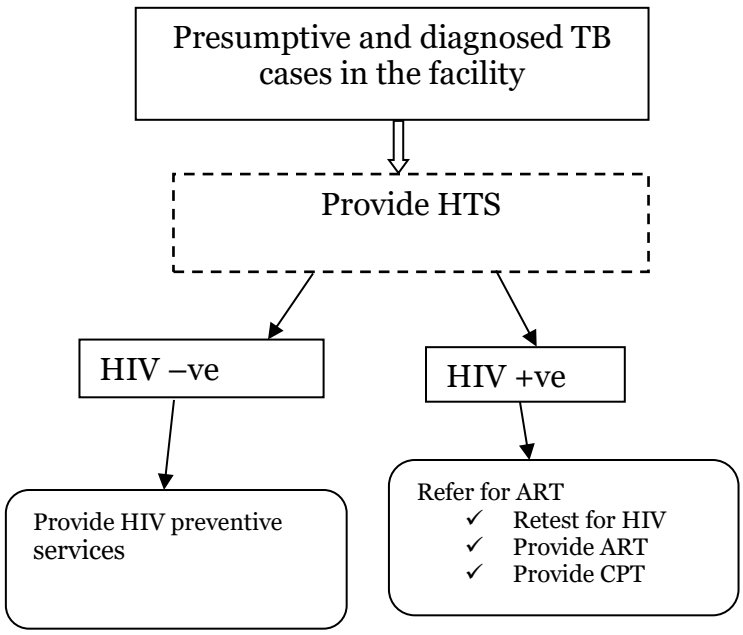


Figure 4: Algorithm for HIV diagnosis and treatment among presumptive and diagnosed TB Cases

All persons who have tested HIV positive should be re-tested prior to the commencement of ART

3.3.1 Laboratory Diagnosis of HIV Infection

Laboratory diagnosis of HIV infection is based on the demonstration of;

- antibodies in plasma or serum.
- viral nucleic acid in the blood.

HIV Rapid Testing Algorithm

The algorithm recommended for routine HIV testing is the serial HIV testing algorithm as shown below:

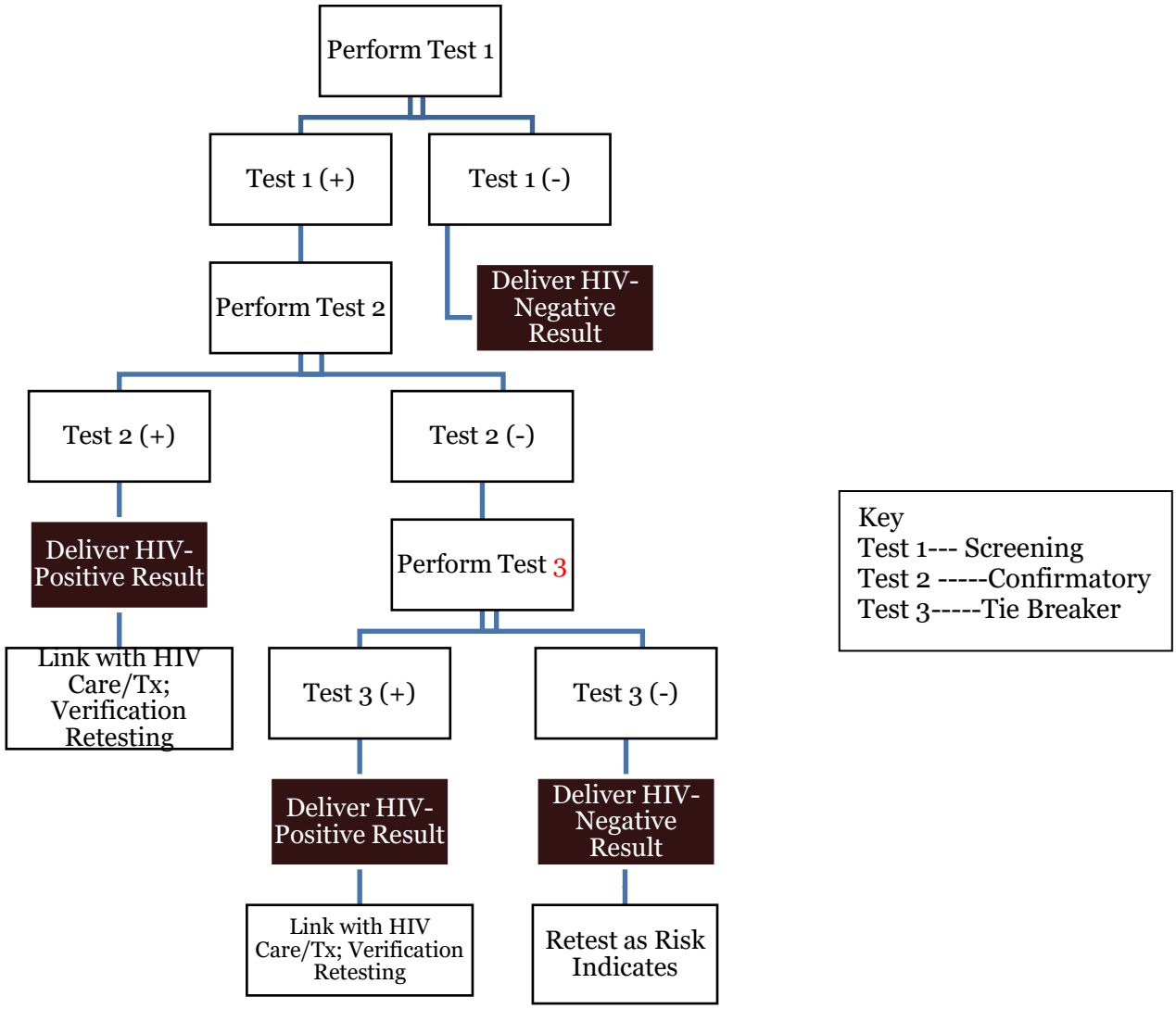


Figure 5: Serial Testing Algorithm

3.3.2 Clinical Staging of HIV Infection

The WHO clinical staging of HIV infection is as shown in Annex 1.

PLHIV with pulmonary TB and extrapulmonary TB are considered WHO stages 3 and 4 respectively.

3.3.3 Antiretroviral Therapy (ART) in TB/HIV Co-infection

There is strong evidence that initiation of ART within two weeks of TB treatment is associated with a marked reduction in overall TB-related morbidity and mortality. ART

should be started in all TB patients living with HIV, regardless of CD4+ cell count. TB treatment should be initiated first, followed by ART as soon as possible within the first 2 weeks of treatment. This strategy will:

- Simplify patient management.
- Improve adherence.
- Avoid ARV and TB drug interactions.
- Avoid overlapping toxicities.

Goals of Antiretroviral Therapy

The goals of ART include:

- Achievement of sustained virologic, immunologic, clinical, and epidemiologic control of HIV.
- Prevention of the development of ARV drug resistance.
- Reduction of morbidity from OIs.
- Improved quality of life.

First-Line ART Regimens for Adults

Table 5: Recommended First-Line ART Regimens for Adults

First-line ART	Preferred first-line regimen	Alternative first-line regimens	Special Circumstances
Adults	TDF + 3TC (or FTC) + DTG	TDF + 3TC (or FTC) + EFV_{400}	TAF + 3TC (or FTC) + DTG ABC + 3TC + DTG AZT* + 3TC + EFV_{400}

3TC: lamivudine; FTC: emtricitabine; ABC: abacavir; AZT: zidovudine; DTG: dolutegravir; EFV: efavirenz; TAF: tenofovir alafenamide; TDF: tenofovir disoproxil fumarate.

Second-Line ART Regimen for Adults

Table 6: Recommended Second-Line ART Regimens for Adult

Target Population	Failing First-line Regimen	Preferred Second-line Regimen	Alternative Second-line Regimens
Adults	TDF+3TC (or FTC) +DTG	AZT+3TC (or FTC) +ATV/r or LPV/r	AZT+3TC (or FTC) +DRV/r
	TDF+3TC (or FTC) +EFV	AZT+3TC (or FTC) +ATV/r or LPV/r	AZT+3TC (or FTC) +DTG
	AZT+3TC (or FTC) +EFV	TDF+3TC (or FTC) +ATV/r or LPV/r	TDF+3TC (or FTC) +DTG

3TC: lamivudine; FTC: emtricitabine; ABC: abacavir; AZT: zidovudine; DTG: dolutegravir; EFV: efavirenz; ATV/r: Atazanavir/ritonavir; LPV/r: lopinavir/ritonavir; TDF: tenofovir disoproxil fumarate.

Table 7: Sequence for switching ART regimens

Target Population	First-line Regimens	Second-line Regimens	Third-line Regimens
Adults and Adolescents	TDF + 3TC (or FTC) + DTG	AZT + 3TC (or FTC) + ATV/r or LPV/r or DRV/r	TDF + 3TC (or FTC) + DRV/r + DTG +/- ETV
	TDF + 3TC (or FTC) + EFV_{400}	AZT + 3TC (or FTC) + ATV/r or LPV/r or DTG or DRV/r	AZT+3TC (or FTC) + DRV/r ± ETV +/- DTG
Children and infants	ABC + 3TC + DTG (children weighing >20kg)	AZT + 3TC + LPV/r (or ATV/r) AZT + 3TC + DRV/r (children > 3years)	RAL or DTG (children weighing >20kg) + DRV/r (children >3years) + ABC or AZT + 3TC
	ABC (or AZT) + 3TC + LPV/r	AZT (or ABC) + 3TC + DTG	

		children weighing >20kg) AZT (or ABC) + 3TC + RAL	
	ABC (or AZT) + 3TC + EFV	AZT (or ABC) + 3TC + DTG (children weighing >20kg) AZT (or ABC) + 3TC + LPV/r (or ATV/r)	

3TC: lamivudine; ABC: abacavir; AZT: zidovudine; DTG: dolutegravir; EFV: efavirenz; FTC: emtricitabine; ATV/r: Atazanavir/ritonavir; LPV/r: lopinavir/ritonavir; DRV: Darunavir; RAL: raltegravir; TAF: tenofovir alafenamide; TDF: tenofovir disoproxil fumarate.

3.4 Special considerations in TB/HIV co-infected patients

A key objective of TB/HIV service integration is to improve the quality of care provided to co-infected patients. The major challenge of managing co-infected patients includes drug-drug interaction, overlapping toxicities between ARVs and anti-TB drugs, adherence to medications as well as Immune reconstitution inflammatory syndrome (IRIS).

3.4.1 Treatment scenarios in adults with TB/HIV co-infection

Possible case scenarios involved in the management of TB/HIV co-infected patient are summarized in the table below:

Table 8: Treatment scenarios involved in the management of TB/HIV co-infected patient

S/N	Scenario	Action
1.	Clients diagnosed with TB/HIV co -	• Start TB treatment • Refer or commence ART.

	infection at presentation	○ Commence ART within 2weeks but not later than 8 weeks of TB treatment initiation irrespective of CD4+ cell count or WHO stage of disease. The need to start ART within 2 weeks of commencement of anti-TB medicine is much more imperative in those with CD4+ cell count < 50 cells/mm^3 • Initiate CPT
2.	Known HIV-positive clients on ART, newly diagnosed with TB	• If on ART for less than 6 months, check for adherence to ART, offer counselling to clients and commence anti-TB treatment immediately • If on ART for more than 6 months, rule out ART failure: ○ Conduct viral load test ○ Commence anti-TB treatment, and if ART failure, manage with the appropriate ARV regimen ○ If no ART failure, continue ART but with modification of regimen as necessary and commence anti-TB treatment - If on DTG or RAL-containing regimen, administer by doubling the dose of DTG or RAL* - If on Atazanavir/ritonavir (ATV/r) or Lopinavir/ritonavir (LPV/r) based ART regimen, substitute Rifampicin with Rifabutin**. If Rifabutin is not available, LPV/r can be used for the duration of the TB treatment by doubling the standard dose of LPV/r (i.e., LPV/r 800/200mg twice daily) - Darunavir use is contraindicated with Rifampicin or Rifabutin

3.	Clients on TB treatment diagnosed with HIV infection	• Considering DTG or RAL containing regimen: - Continue first line anti-TB medicines - Double DTG or RAL* dose by administering same dose twice daily • Considering LPV/r or ATV/r-based regimen: - Replace Rifampicin with Rifabutin** and administer anti-TB medicines as loose drugs - Considering Efavirenz (EFV) based regimen for children greater than 3 years: - Continue first - line rifampicin containing anti - TB medicines without dosage adjustment

****RAL is to be used for children***

*****Rifabutin is obtainable through the State TB and Leprosy Control Programmes; refer to Annex 2 for SOP for Rifabutin use in TB/HIV co-infected patients requiring protease inhibitor-based ARV.***

3.4.2 ARV and anti-TB drug interaction

Drug interactions may occur when ARV drugs and anti-TB medicines are co-administered. Some of these interactions and actions to take are illustrated in table 10 below.

Table 9: ARV and anti-TB drug interactions and actions to take

Drug	Interaction	Action
Rifampicin	Decreases plasma level of all PIs by at least 75% (except ritonavir, which it decreases by 35%). Rifampicin also decreases plasma levels of EFV (25%), and NVP (20%–58%) and DLV (96%)	Rifampicin should not be co-administered with DRV. Modify the doses of LPV/r when co-administered with Rifampicin Rifampicin can be administered with EFV. Maintain EFV dose at 600

	Rifampicin lowers plasma concentration of DTG	mg once daily and monitor for virologic response. It is preferable that Rifampicin should not be co-administered with NVP. Give DTG 50mg twice daily
Rifabutin	It decreases levels of all PIs and NNRTIs by 15 to 35%, LPV/r increases Rifabutin level by 300%; ATV increases Rifabutin level by 250% EFV decreases Rifabutin level by 38%.	Rifabutin dosage should be reduced to 150 mg od when co-administered with LPV/r, ATV or ATV/r Rifabutin dose should be increased to 450–600 mg once daily or 600 mg three times a week
Bedaquiline	Efavirenz decreases the concentration of Bedaquiline by 50%	Replace Efavirenz with another suitable ARV drug such as DTG or LPV/r

3.4.3 Overlapping ARV and TB drug side effects

Concurrent use of ARVs and anti-TB drugs have a potential for additive toxicity. Some of the common ones are:

- Skin rashes: Nevirapine / Efavirenz – Pyrazinamide / Isoniazid / Rifampicin -
- Peripheral neuropathy: NRTIs - Isoniazid

  These overlapping side effects make it difficult to identify the causative drug when a patient is receiving treatment for both TB and HIV concurrently.

3.4.4 Immune Reconstitution Inflammatory Syndrome

Immune Reconstitution Inflammatory Syndrome (IRIS) is a spectrum of clinical signs and symptoms that is associated with immune recovery brought about by a response to ART. It usually occurs within the first 4–8 weeks after initiating ART and is characterized by worsening of:

- Symptoms or signs such as high fever, lymphadenopathy central nervous system lesion
- Radiological features of TB such as consolidations, cavities, pleural effusion.

Risk factors for TB IRIS

- Non-recognition and/or inadequate therapy for pre-existing OIs before initiation of ART
- Low CD4+ cell count (<50 cells/mm3) at ART initiation
- Disseminated OIs or tumors

Important steps to reduce the development of IRIS

- Early HIV diagnosis and initiation of ART before a decline to <200 cells/mm^3
- Improved screening for OIs before ARVs especially TB and Cryptococcus
- Optimal management of OIs before initiation of ART.

Management of TB IRIS

- Rule out other conditions that can mimic TB IRIS (e.g., pulmonary histoplasmosis, other OIs)
- Provide supportive care and anti-inflammatory therapy if required e.g., steroid
- Continue ART and anti-TB medications

Note:

If an episode of TB develops after the initiation of ART, refer the patient to a medical officer for appropriate management.

Refer patients with suspected TB IRIS to medical officers for appropriate management.

3.4.5 Adherence to Drugs

In TB/HIV co-infection, optimal adherence to therapy is essential to achieve good treatment outcome. The increased pill burden (Anti-TB, ART, CPT and other OI medications) poses a great challenge to achieving optimal adherence. Co-infected patients should be adequately counseled for adherence before initiating treatment. For optimal virological suppression adherence rates exceeding 95% is necessary. All efforts should be made to identify and address common potential barriers to adherence such as:

- Poor patient-healthcare worker relationship.
- High pill burden.
- Depression.
- Lack of Social support.
- Substance abuse including alcohol.
- Lack of motivation regarding adherence.
- Lack of patient education.
- Inability of patients to identify their medications.
- Drug toxicity.
- Stigma and discrimination.
- Non-disclosure of HIV status.
- Distance to health facilities.

Adherence is crucial for delaying or preventing the development of drug resistance, reducing the risk of transmitting HIV and ensuring maximum durability of the first-line ARV regimen. Some of the strategies that should be taken before initiation and during therapy to ensure optimal adherence include:

- Treatment education for patients and treatment supporters.
- Treatment supporter's involvement for ART and TB DOTS.
- The use of peer health educator to ensure adherence.
- Directly Observed Therapy for ARV and anti-TB drugs.
- Simple drug regimen e.g., Fixed dose combination.
- Use of reminders (e.g., a cell phone, alarm clock).
- Synchronize the ART and TB DOT clinic appointment where possible.

3.4.6 Management of TB/HIV in Special Circumstances

Advanced HIV Disease (AHD)

Advanced HIV Disease **(**AHD) in adults, adolescents, and children older than five years is defined as PLHIV with CD4 cell count <200cells/mm3 or WHO stage 3 or 4. All children younger than five years living with HIV are considered to have AHD.

It is recommended:

- That Urine LF-LAM and Xpert MTB/RIF assay be used to diagnose TB in AHD (see annex 3 Algorithm for LF-LAM and Xpert MTB/RIF assay in PLHIV).
- To commence ART within 2weeks but not later than 8 weeks of TB treatment irrespective of CD4+ cell count or WHO stage of disease. The need to start ART within 2 weeks of commencement of anti-TB medicine is much more imperative in those with CD4+ cell count < 50 cells/mm^3.

Pregnancy

All pregnant TB/HIV co-infected patients should be managed in the same way as adults. However, cotrimoxazole prophylaxis should be avoided in 1st trimester of pregnancy.

The recommended ART regimen for pregnant women is TDF + 3TC + DTG.

Note:

- Rifabutin has no sufficient data to support safety in pregnancy and breastfeeding.

Renal Failure

For TB/HIV co-infected patients with renal failure or undergoing dialysis:

- Rifabutin: No dose adjustment in mild renal insufficiency. For creatinine clearance of <30 ml/minute, the usual dose may be used, but monitor drug concentration to avoid toxicity.
- Rifampicin: No dose adjustment is required.
- Isoniazid: Give Isoniazid 300mg once daily or 900mg three times weekly.
- Pyrazinamide: Give Pyrazinamide at 25mg/kg/dose, three times per week.
- Ethambutol: Give Ethambutol at 15 – 25mg/kg/dose three times weekly.

- Tenofovir disoproxil fumarate (TDF): Discontinue in patients with renal failure and replace with less nephrotoxic ARVs like abacavir and tenofovir alafenamide (TAF).

Liver Diseases

For TB/HIV co-infected patients diagnosed with liver diseases:

- All first line anti-TB medicines should be used with caution in patients with liver diseases except ethambutol (with minimal effect on the liver enzymes)
- Dolutegravir (DTG) can cause hepatotoxicity, hence it is recommended to monitor liver function and toxicity as it may worsen with existing hepatitis B or C.

Diabetes Mellitus

Diabetes Mellitus (DM) can impair the immune system, a risk factor for developing TB disease. Diabetic patients with TB/HIV co-infection are at risk of poorer treatment outcomes. The presence of DM may potentiate the adverse effects of anti-TB drugs especially in presence of renal dysfunction and peripheral neuropathy. However, none of the anti-TB drugs are contra-indicated.

Note:

Caution should be taken with the use of PIs in patients with Diabetes Mellitus, as this can increase the blood sugar level.

CHAPTER FOUR
Management of TB/HIV Co-infection in children and adolescents

4.1 Introduction

HIV infected children and adolescents have higher risks of acquiring TB infection, faster disease progression and TB-related morbidity and mortality. A high index of suspicion is required for identifying clinical features of active TB disease in children with HIV.

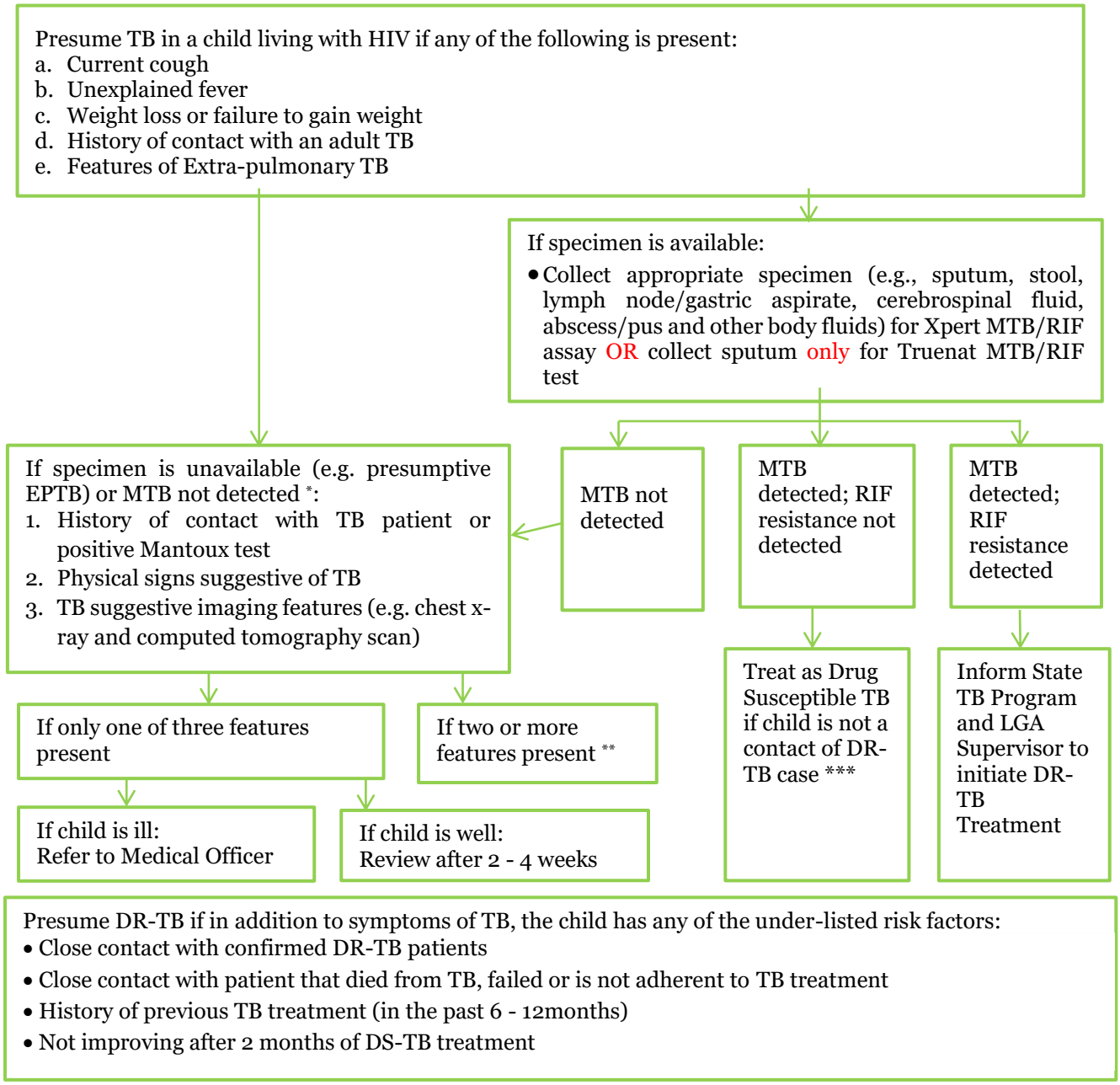
4.2 Management of TB in children and adolescents with HIV

The key risk factors for TB in children and adolescents include:

- Household or other close contact with a case of pulmonary TB.
- Age < 5 years.
- HIV infection.
- Severe malnutrition.

4.3 Diagnosis of TB in children and adolescents living with HIV

The approach to diagnosing TB in children and adolescents with HIV infection is as shown in the algorithm below.



**** Clinical diagnosis is recommended if all effort at bacteriological confirmation using Xpert MTB/RIF assay/Truenat test (or Urine LF - LAM assay in PLHIV with advanced disease) is not possible.***

***** In settings where there is no doctor (e.g., hard to reach areas), the trained health care worker can make a diagnosis of TB and commence anti - TB treatment.***

****** Treat as DR-TB if child is a contact of DR-TB case***

Figure 6: Algorithm for Diagnosing Pulmonary and Extra-Pulmonary TB in Children and Adolescents

There could however, be some challenges in applying this approach in children and adolescents with HIV infection. These challenges are as outlined below:

- Poor sensitivity of TST for identifying TB infection
- Lower specificity and sensitivity of clinical features: clinical overlap between symptoms of TB and HIV, malnutrition and advanced immunosuppression
- Difficulty in sample collection
- Low MTB yield in samples (pauci-bacillary disease)

4.4 Investigations for diagnosing TB in children and adolescents living with HIV

The under-listed investigations are recommended for diagnosing Child and Adolescent TB.

a). Bacteriological investigations: Xpert MTB/RIF assay is the first-line test for diagnosing TB. Other bacteriological tests include Truenat MTB-RIF Dx, culture and DST, first and second-line Line Probe Assay (LPA) and urine LF - LAM assay

As a result of difficulty of collecting sputum in children, other specimens including stool, gastric aspirate/lavage, stool, cerebrospinal fluid (CSF), lymph node aspirate, biopsy specimens, pleural or ascitic fluid, joint aspirate can be sent for Xpert MTB/RIF assay.

Note:

- **Stool for Xpert MTB/RIF assay is particularly useful for diagnosing pulmonary and gastro-intestinal TB in children.**
- **Xpert MTB/RIF assay may be positive in less than one third of children with TB. Therefore, a negative result does not rule out TB. There may be need for clinical diagnosis using clinical features, radiological and other supportive investigations.**
- **For the use of LF- LAM refer to chapter 3.**

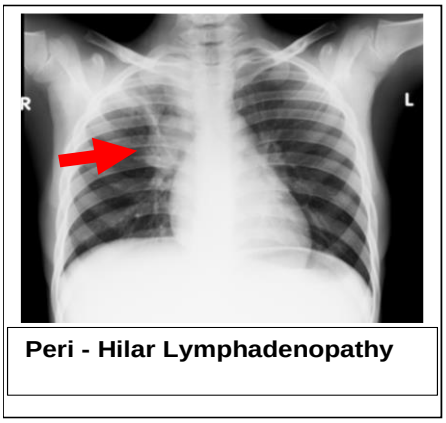
b). Radiological Investigations

i) Chest x-ray

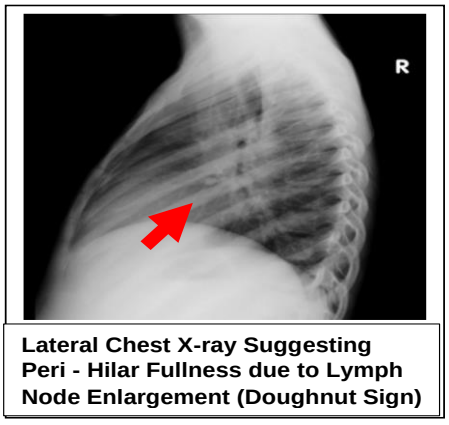
Chest X-ray is an important tool for the diagnosis of TB in children, many of whom are Xpert MTB/RIF negative.

- Chest x-ray is important in evaluating children for TB (even of extra-pulmonary form) as the portal of entry of the bacilli into the body is the lungs in greater than 95% of cases.
- In a child with no signs of respiratory difficulty (no fast breathing or chest in-drawing), chest X-ray findings may still be supportive of TB diagnosis.
- A normal chest x-ray finding does not necessarily exclude pulmonary TB

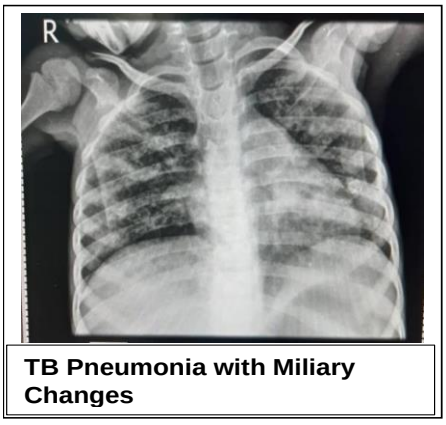
Common chest X-ray abnormalities suggesting TB in children living with HIV are as shown below:



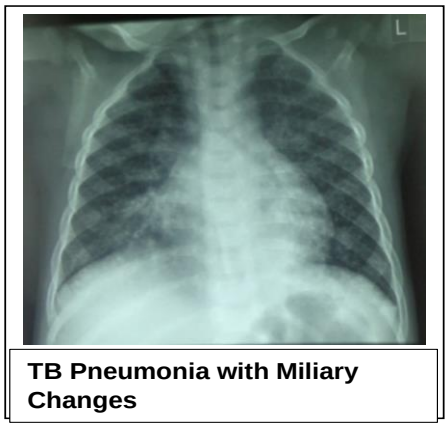
Peri - Hilar Lymphadenopathy



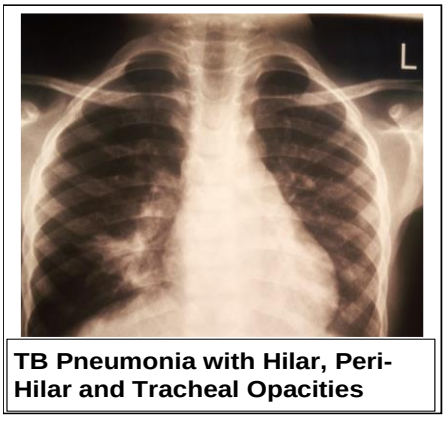
Lateral Chest X-ray Suggesting Peri - Hilar Fullness due to Lymph Node Enlargement (Doughnut Sign)



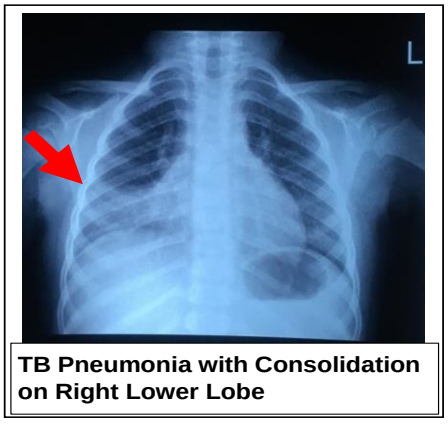
TB Pneumonia with Miliary Changes



TB Pneumonia with Miliary Changes



TB Pneumonia with Hilar, Peri-Hilar and Tracheal Opacities



TB Pneumonia with Consolidation on Right Lower Lobe

Figure 7: Common Chest X-ray Findings Suggesting TB in Children Living with HIV

ii) Other Radiological Investigations:

These include ultrasound scan (USS), Computed Tomography (CT) scan and Magnetic Resonance Imaging (MRI) and the indications for use of each tests depend on the parts of the body involved.

c). Other Supportive Investigations

ii) **Histology**: Histology of appropriate tissue such as lymph node, pleura and other appropriate tissues.

4.5 Extra - pulmonary TB in Children and Adolescents with HIV

EPTB is common in children and presentation varies with age. Clinical features vary depending on site of disease.

Diagnosis of EPTB in children and adolescents may be made by:

- Positive bacteriological result
- Clinical evidence consistence with EPTB.

For details of forms and Evaluation of EPTB, refer to Chapter 3.

4.6 Classification of TB in Children and Adolescents

The approach for classifying TB in children is the same as that of adults. Refer to Chapter 3.

4.7 Treatment of TB in Children and Adolescents Living With HIV

The principle of TB treatment in HIV positive children and adolescents with TB is essentially the same as that of adult.

4.7.1 Preparing Children and Adolescents for Anti-TB Therapy

Preparing children and adolescents living with HIV before commencing anti-TB therapy is very important for the following reasons:

a. To ensure adherence to both anti-TB and anti-retroviral medicines.
b. To achieve cure for TB infection and disease.
c. To prevent development of relapse and drug resistance.

HCWs should provide the followings:

- Health education on the diagnosis, available treatment modalities, duration of treatment and likely adverse effect of treatment.
- Counselling for children and adolescents, parents/care givers on the need for adherence to both clinic appointments and medications e.g., anti-TB, ART and CPT.
- Ensure identification of treatment supporter/responsible care giver.
- Ensure counselling on nutrition and caregivers understand the need for provision of adequate diet to facilitate recovery and catch-up growth.

4.7.2 Administering TB Treatment

The recommended route for administering anti-TB medicines is oral. Two standardized child-friendly treatment regimens have been adopted for the treatment of all children diagnosed with susceptible TB. These regimens include the following:

1. Regimen 1-**2(RHZ+E)/4(RH).** Six months treatment regimen for children with all forms of TB except TB meningitis and Osteo-articular TB.
2. Regimen 2- **(RHZ+E)/10(RH).** Twelve months treatment Regimen for all children with TB meningitis and Osteo-articular.

Table 10: Medicine Dosing for Children with Drug Susceptible PTB/EPTB cases*

	Pre-treatment weight (Kg)					
Daily Regimen	**< 4**	**4 – 7**	**>7 – 11**	**>11-15**	**>15 - <25**	**≥ 25**
Intensive phase (2 months)						
• Combined tablets: RHZ (75mg+50mg+150mg)	½	1	2	3	4	
						Adult tablets
• Ethambutol tablet (100mg)	½	1	2	3	4	
Continuation phase (4 months)						
• Combined tablets: RH (75 mg + 50 mg)	½	1	2	3	4	

****Refers to all PTB and EPTB cases except TB meningitis, miliary TB and* **Osteo-articular TB.**

*** *Rifampicin may cause orange/red coloured urine and other body fluids. Counsel and reassure on side effect and encourage increased fluid intake.***

Table 11: Medicine Dosing for Children with TB Meningitis, Miliary and Osteo-articular TB

	Pre-treatment weight (Kg)					
Daily Regimen	**<4**	**4 - 7**	**>7 – 11**	**>11 – 15**	**>15 - <25**	**≥ 25**

Intensive phase (2 months)						
• Combined tablets: RHZ (75mg+50 mg+150 mg)	½	1	2	3	4	Adult tablets
• Ethambutol tablet (100mg)	½	1	2	3	4	
Continuation phase (10 months)						
• Combined tablets: RH (75mg+50mg)	½	1	2	3	4	

Figure 8: How to Administer the Child-friendly TB medicines

Note:

- Streptomycin is no longer recommended for Drug Susceptible TB treatment.
- Breastfeeding infants and children should continue to breastfeed while receiving anti-TB treatment.

• Directly Observed Therapy (DOT) is the hallmark of anti-TB treatment.

Many children rapidly gain weight after initiation of TB treatment. It is important to monitor the child's weight at every clinic visit and to adjust medicine doses accordingly.

4.7.3 Use of Adjuvant Therapy in TB treatment

Adjuvant therapy in TB treatment includes:

a. Steroids: Steroids are indicated in the following conditions:

- Meningitis
- Pericarditis
- Lymph node involvement with pressure effect
- Large pleural effusion
- Other forms of EPTB as specified in Chapter 3.

Either prednisolone (1mg/kg wt. {max 40mg} in children for an initial period of 21 days followed by tapering off by 25% per week over four weeks) or dexamethasone may be used.

b. Pyridoxine (vitamin B6) should be given orally to all children on TB treatment to protect against isoniazid-induced peripheral neuropathy; 1.2mg per kg not exceeding 50mg per day

Table 12: Dosage of Pyridoxine in Children and Adolescents

S/N	Age	Dosage
1.	Less than 4 years	12.5mg daily
2.	4 years and above	25mg daily

4.7.4 Adverse Effects of Anti - TB medicines

Adverse effects of anti - TB medicines in children and adolescents is similar to that of adults; though less common. The symptom-based approach to managing side effects of First line anti-TB medicines is described below.

Table 13: Symptom-based Approach to Managing Adverse effects of First line Anti-TB Medicines

Type	Adverse effects	Actions
Major Adverse effects	• Severe skin rash with or without itching • Jaundice (other causes excluded) • Hepatitis • Visual impairment (other causes excluded) • Shock, bleeding, kidney failure • Abnormal behaviour (psychosis) • Convulsions	• Stop anti - TB medicines. • Refer immediately to a Medical Officer/Paediatrician
	• Anorexia • Nausea • Abdominal pain	• Give drugs with small meals or just before bedtime. • Advise patient to swallow pills slowly with small sips of water. If symptoms persist/worsen, refer to hospital.
	• Burning/numbness in hand and/or feet	• Tabs pyridoxine daily
	• Joint pains	• Non-steroidal anti- inflammatory drug (e.g., Ibuprofen) or paracetamol.
	• Drowsiness	• Reassurance. Give drugs before bedtime.

4.8 Monitoring of TB Treatment in Children

The approach for Monitoring TB Treatment in Children is the same as that of Adults as described in Chapter 3.

4.9 Treatment Interruption in children

TB treatment interruption in children is similar to that of Adults as described in chapter 3

4.9.1 Poor Response to Treatment

Most children with TB will start to show signs of improvement after 2 to 4 weeks of commencing anti-TB treatment. Poor adherence is a common cause of poor response and eventual treatment failure.

Consider treatment failure in a child who is receiving anti - TB treatment and has one or more of the following:

- No symptom resolution, or symptoms are getting worse.
- Poor weight gain/continuing weight loss.
- AFB sputum smear-positive at 5 month or more follow-up sputum.

Treatment failure is more common in HIV-infected children. Treatment failure suggests the possibility of DR -TB and needs careful assessment.

4.10 Treatment Outcome

TB treatment outcome in children is similar to that of Adults as described in Chapter 3.

4.11 Prevention of TB in children

Strategies for preventing TB include:

- Bacille Calmette-Guerin (BCG) vaccination in the new-born
- Contact investigation and management.
- TB Preventive Therapy (TPT).
- Infection Control Measures at community and facility levels such as cough etiquette, avoiding over-crowding and ensuring good cross ventilation both at health facilities and homes.
- General measures such as early identification and prompt treatment of diagnosed TB cases, good personal hygiene, maintaining good nutrition.

4.12 TPT in children and Adolescents Living with HIV

TB preventive therapy is an important intervention in preventing development of active TB. Refer to Chapter 7 for details on TPT.

4.13 Antiretroviral Therapy in children and Adolescents with TB

ART is a life saving measure in children and adolescents with TB/HIV co-infection. Early initiation of ART in co-infected children and adolescents reduces morbidity and mortality associated with the rapid disease progression and helps maintain normal growth and development.

4.13.1 Initiating ART in Children and Adolescents

ART should be initiated in all children and adolescents living with HIV, regardless of WHO clinical stage and CD4+ cell count (Refer to annex 1 for HIV staging). However, priority for ART initiation should be given to those with AHD.

4.13.2 Recommended ART Regimen for Children and Adolescents

The following are the recommended ART regimens for the management of HIV in Children and Adolescents.

Table 14: Recommended First-line ART regimen for Neonates, Infants, and Children

Weight (Kg)	**Age (years)**	**Preferred First Line Regimen**	**Alternative First Line Regimen**	**Special Circumstances**
Neonates				
< 3kg	< 1 month	AZT + 3TC + DTG* or RAL	AZT + 3TC + LPV/r**	AZT+3TC+NVP
Infants & Children				
< 20kg	< 6years	ABC +3TC + DTG	ABC+3TC +LPV/r AZT + 3TC +LPV/r	

			ABC (or AZT) +3TC+ RAL	ABC + 3TC +EFV*+ (or NVP) AZT + 3TC + EFV (or NVP) AZT + 3TC + LPV/r (or RAL)
20 – 30kg	6-10years	ABC+3TC+DTG Or TDF***(TAF)**** + 3TC +DTG	ABC+3TC +LPV/r ABC +3TC + RAL	

Note:

****DTG 5mg is used in younger children from 4weeks of age and weighing at least 3kg and 10mg dispersible is used for children <20kg***

*****LPV/r pellets or granules can be used if starting after two weeks of age***

******TDF is used for children aged 6-10 years weighing >30kg***

*******TAF is used for children with weight >25kg***

****+EFV is used for children above 3years (>15kg)***

The use of this INSTI could be considered where available in instances of poor tolerability or administration challenges with LPV/r, particularly in settings where the rapid expansion of maternal treatment could lead to infants and children at very high risk of carrying an NNRTI resistance virus.

Table 15: Recommended Second-line ART Regimen for Neonates, Infants, and Children

Weight (Kg)	**Age (years)**	**Failing First Line Regimen**	**Preferred 2nd Line Regimen**
Neonates			
< 3 kg	< 1 month	AZT + 3TC + DTG or RAL	AZT + 3TC + LPV/r
Infants & Children			
< 20kg	< 6years	ABC +3TC + DTG	AZT+ 3TC + LPV/r or ATV/r*** ABC+3TC +LPV/r

			ABC (or AZT) +3TC+ RAL AZT+3TC+DRV/r
20-30kg	6 – 10years	ABC+3TC+DTG OR TDF* (TAF**) + 3TC (or FTC) + *DTG	AZT + 3TC + LPV/r or ATV/r ABC +3TC + LPV/r or ATV/r AZT+3TC+DRV/r

TDF is used for children aged 6-10 years weighing >30kg

****TAF is used for children weighing > 25kg***

*****ATV/r can be used as an alternative to LPV/r for children older than 3months, but limited availability of suitable formulations for children younger than 6years***

Table 16: Sequence of Switching ART from first-Line to third-line regimens

Target Population	**First-line Regimens**	**Second-line Regimens**	**Third-line Regimens**
Children and infants	ABC + 3TC + DTG (children weighing >20kg)	AZT + 3TC + LPV/r (or ATV/r) AZT + 3TC + DRV/r (children > 3years)	RAL or DTG (children weighing >20kg) + DRV/r (children >3years) + ABC or AZT + 3TC
	ABC (or AZT) + 3TC + LPV/r	AZT (or ABC) + 3TC + DTG children weighing >20kg) AZT (or ABC) + 3TC + RAL	

	ABC (or AZT) + 3TC + EFV	AZT (or ABC) + 3TC + DTG (children weighing >20kg) AZT (or ABC) + 3TC + LPV/r (or ATV/r)	

Table 17: Recommended first-line ART regimens for adolescents, pregnant, breastfeeding women and children

First-line ART	Preferred first-line regimen	Alternative first-line regimens	Special Circumstances
Adolescent	TDF + 3TC (or FTC) + DTG	TDF + 3TC (or FTC) + EFV400	TAF + 3TC (or FTC) + DTG ABC + 3TC + DTG AZT + 3TC + EFV400

Table 18: Preferred and Alternative Second-line ART regimens for Adolescents

Target Population	Failing First-line Regimen	Preferred Second-line Regimen	Alternative Second-line Regimens
Adolescents	TDF+3TC (or FTC) +DTG	AZT+3TC (or FTC) +ATV/r or LPV/r	AZT+3TC (or FTC) +DRV/r
	TDF+3TC (or FTC) +EFV	AZT+3TC (or FTC) +ATV/r or LPV/r	AZT+3TC (or FTC) +DTG

	AZT+3TC (or FTC) +EFV	TDF+3TC (or FTC) +ATV/r or LPV/r	TDF+3TC (or FTC) +DTG

Table 19: Sequence of Switching ART from first-Line to third-Line regimens

Target Population	First-line Regimens	Second-line Regimens	Third-line Regimens
Adolescents	TDF + 3TC (or FTC) + DTG	AZT + 3TC (or FTC) + ATV/r or LPV/r or DRV/r	TDF + 3TC (or FTC) + DRV/r + DTG +/- ETV
	TDF + 3TC (or FTC) + EFV 400mg	AZT + 3TC (or FTC) + ATV/r or LPV/r or DTG or DRV/r	AZT+3TC (or FTC) + DRV/r ± ETV +/- DTG

4.14 Adherence to ART among children and adolescents

Adherence among children and adolescents is a special challenge due to a number of peculiarities including:

- Limited choice of paediatric ART formulations.
- Poor palatability of liquid formulations.
- High pill/liquid burden.
- Large pill size and difficulties in swallowing tablets.
- Frequent dosing requirements.
- Dietary restrictions.
- Loss of primary caregiver.
- Adverse drug effects..

Successful therapy for TB as well as HIV requires the commitment and involvement of a responsible caregiver. Parents and other family members of children with HIV may themselves be living with HIV and suboptimal HIV care and treatment for family members could result in sub-optimal care for the child.

4.15 Treatment of TB/HIV Co-infection in children and adolescents

A comprehensive approach to diagnosis and integrated (family/household centred) management of both TB and HIV is critical. The success of TB/HIV co-infection management is linked to the selection of ARV regimen compatible with TB therapy. TB/HIV co-infection in children should be managed as follows:

- Anti - TB treatment should be commenced at least 2 weeks before initiating anti-retroviral therapy (ART).
- Ensure regular follow up and start co-trimoxazole preventive therapy (CPT) if there is no contraindication.
- All HIV-positive children irrespective of age should receive TPT if there is no contraindication after TB disease has been treated or excluded.
- Health care workers should counsel clients, caregivers and family members for optimal adherence as well as provide psychosocial and nutritional support.
- Counsel and test all family/household members for HIV and TB.
- Patients should be weighed at regular intervals and dosages should be adjusted as appropriate for weight.

Refer to chapter 3 for possible scenarios involved in the management of TB/HIV co-infected children.

Note:

Drug interactions between Rifampicin and protease inhibitors or Nevirapine makes co-treatment in children < 3 years challenging, but use of triple NRTI has been shown to be efficacious and offers a suitable option for those in need of TB treatment while on ART

4.16 Special situations in the management of TB/HIV co-infection in children

The special situations involved in the management of TB/HIV co-infection in children is the same as that of adults. Refer to Chapter 3.

CHAPTER FIVE
Tuberculosis Preventive Treatment in PLHIV

5.1 Introduction

Tuberculosis Preventive Treatment (TPT) is the use of anti-TB medicines to prevent the development of active TB among PLHIV. TPT reduces HIV associated TB death and is therefore recommended as part of care package for PLHIV without active TB.

5.2 Screening PLHIV for TPT

It is recommended that all PLHIV are screened at every encounter for TB in order to determine the eligibility for TPT. Refer to the algorithms below.

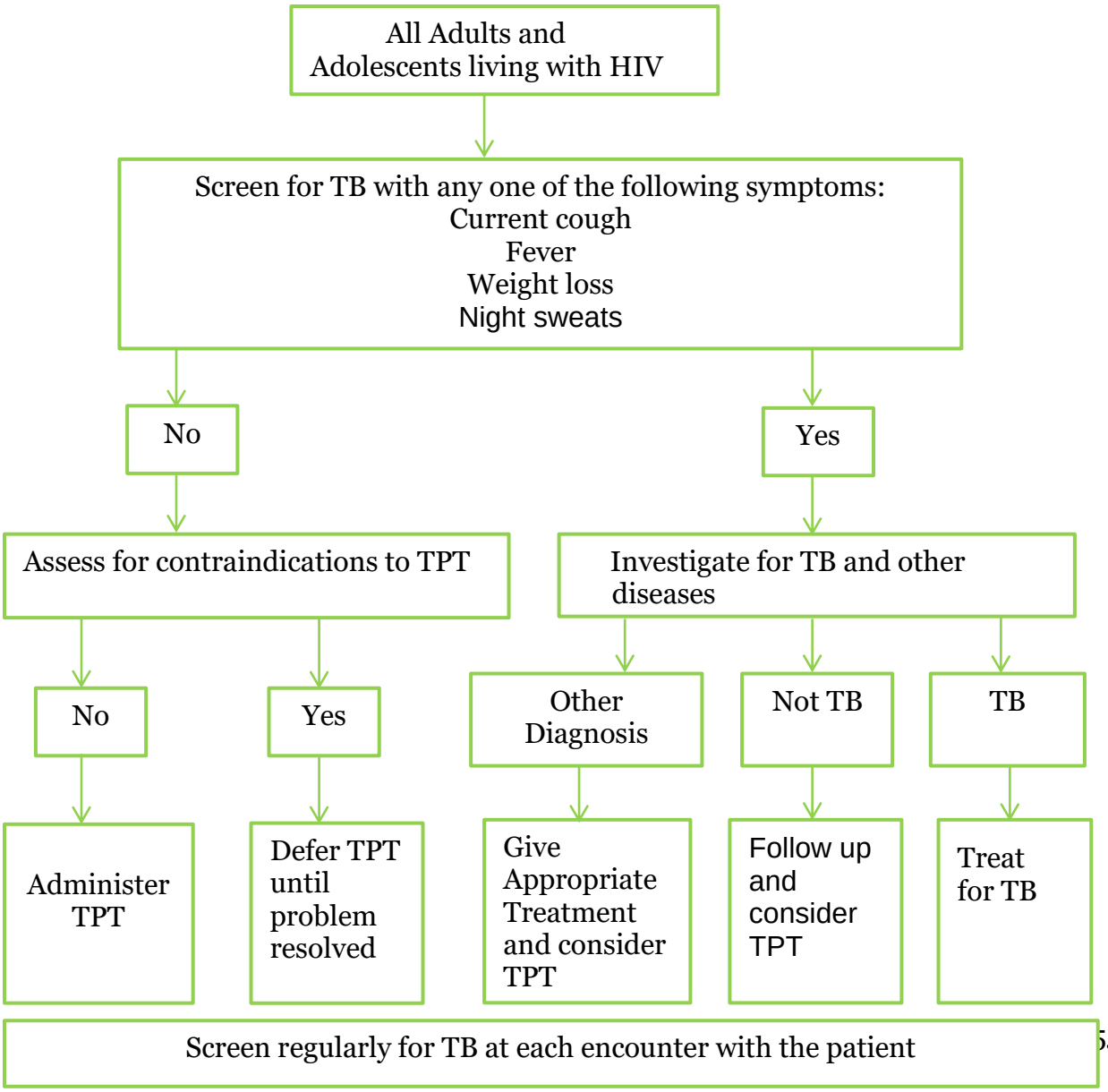
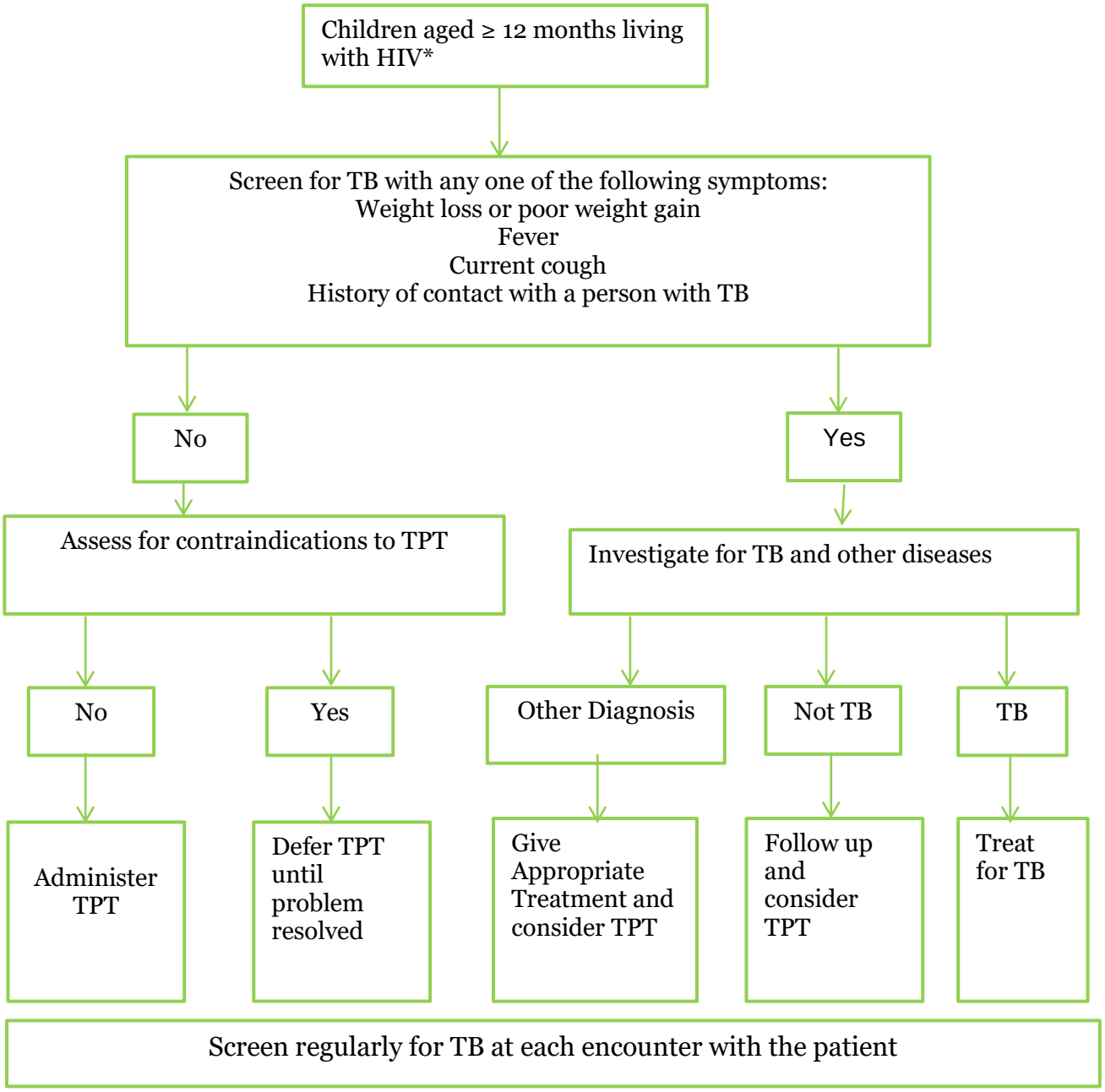


Figure 9: Algorithm for Screening Adults and Adolescents Living with HIV for TPT



****All infants < 1 year should only be given TPT if they have a history of household contact with a TB case and do not have active TB after evaluation.***

Figure 10: Algorithm for Screening Children aged ≥ 1 year Living with HIV for TPT

5.3 Steps in Commencing TPT

The following steps should be followed before placing PLHIV on TPT

- Verify/Confirm HIV Status
- Exclude active TB
- Exclude TPT contraindications
- Counsel on the followings:
  - TPT adherence
  - Side effects of the medicines
  - Immediate recognition and reporting of symptoms of active TB
- Commence TPT, if no contraindication

5.4 TPT regimen

The following options are recommended to be used as TPT:

- 6 months of daily isoniazid (6H)
- 3-month regimen of weekly Rifapentine plus Isoniazid (3HP)
- 3-month regimen of daily Isoniazid plus Rifampicin. (3HR)
- 1-month regimen of daily Rifapentine plus Isoniazid (1HP)

The recommended dosages of medicines used for TPT is shown in Table 20 below:

Table 20: Recommended Dosages of Medicines used for TPT

TPT regimen	**Dose per kg body weight in children**	**Maximum dose**
Isoniazid alone daily for 6 months (6H)	10mg (range: 7 - 15mg)	300mg
Weekly Rifapentine plus Isoniazid for 3 months -12 doses (3HP)	**Isoniazid:** Individuals aged ≥ 12 years - 15mg Individuals aged 2 - 11 years - 25mg **Rifapentine:** 10.0 - 14.0 kg = 300mg	Isoniazid - 900mg Rifapentine - 900mg

	14.1 - 25.0 kg = 450mg 25.1 - 32.0 kg = 600mg 32.1 - 50.0 kg = 750mg > 50 kg - 900mg	
Daily Isoniazid plus Rifampicin for 3 months (3HR)	**Rifampicin:** Age < 10 years = 15mg (range: 10 – 20mg) Age ≥ 10 years = 10mg **Isoniazid:** Age < 10 years = 10mg (range: 7 – 15mg) Age ≥ 10 years = 5mg	Rifampicin - 600mg Isoniazid - 300mg
Daily Isoniazid and Rifapentine for 1 month	**Age ≥ 13 years (regardless of weight band)** Isoniazid 300 mg/day Rifapentine 600 mg/day	Isoniazid – 300mg Rifapentine - 600mg

A triple pill combination containing Isoniazid + Cotrimoxazole + Pyridoxine (scored) is available (1 pill daily for adults, half pill for children 5 years and older of age and quarter for children < 5 years of age).

For clients that will be eligible for this fixed dose combination, care should be taken not to prescribe cotrimoxazole again.

a) Dosage of Isoniazid (INH)

i) **Dosage of INH for TPT in children:** INH is administered daily for TPT in children for a total duration of 6 months as stated in Table 21 below

Table 21: Dosage of INH for TPT in Children

Weight in kg	INH dosages in mg/day	INH in Tablet/day
<2.5	25	¼ of 100mg tablet
2.5 - 5.9	50	½ of 100mg tablet
6.0 - 10.9	100	1 of 100mg tablet
11.0 - 25.0	150	1½ of 100mg tablet

ii) **Dosage of INH for TPT in adults**: INH is administered daily for TPT in adults at a dose of 300mg daily for a total duration of 6 months.

b) Dosage of 3HR for TPT in adults and children

The dosage of 3HR for TPT in adults and children is as shown in Table 22 below

Table 22: TPT Dosage of 3HR

Children **Strength: RH* 75mg/50mg FDC****		**Adult** **Strength: RH 150mg/75mg FDC**	
Weight Band	**RH Tablets**	**Weight Band**	**RH Tablets**
4 - 7 kg	1	25 - 37 kg	2
8 - 11kg	2		
12 - 15kg	3	38 - 54 kg	3
16 - 24kg	4		
≥ 25kg	Use adult Regimen	≥ 55kg	4

* ***RH - Rifampicin and Isoniazid***

** ***FDC - Fixed Dose Combination***

c) Dosage of 3HP for TPT in adults and children

Dosage of 3HP in adults: The dosage of 3HP in adults is as shown in Table 23 below

Table 23: Dosage of FDC of 3HP for TPT in adults

Medicine	Formulation	Weight bands for patients >14 years				
		30 - 35kg	36 - 45kg	46 - 55kg	56 - 70kg	> 70kg
Isoniazid	300mg	3	3	3	3	3
Rifapentine	150mg	6	6	6	6	6

Dosage of 3HP in children: The dosage of 3HP in children is as shown in Table 24 below

Table 24: TPT Dosage of 3HP for Children Aged 2 - 14 years*

Weight	Rifapentine** (150mg tablets)		Isoniazid (100mg tablets)	
	Dose	Tablets	Dose	Tablets
10 - 15 kg	300mg	2	300mg	3
16 - 23 kg	450mg	3	500mg	5
24 - 30kg	600mg	4	600mg	6
> 31kg	750mg	5	700mg	7

****Patient aged 15 years and older should receive adult dosing***

*****Rifapentine has a bitter taste. For young children who cannot swallow, crush the tablet and mix with small amount of multivitamin syrup***

Note:
In patients with severe malaria (impaired consciousness, low blood glucose, jaundice, kidney failure, anaemia and parasitaemia >10%), stop 3HP, treat malaria urgently. Restart 3HP once the episode of Malaria is resolved, to avoid drug-drug interactions

Contraindication to use of 3HP

- Individuals who have had prior adverse events or hypersensitivity to INH or Rifapentine.
- Known pre-existing liver damage.
- Children under two years (no dosing for children < 2years).

Note:

- Supplement with Pyridoxine daily for six months;
  - Adults 25-50mg
  - Children: less than 4 years =12.5mg, 4 years and above = 25mg
- TPT appointment date should be aligned as much as possible with that of ART to reduce frequency of visit
- Pre-pack TPT medicines for the complete course before commencing clients on TPT
- Once weekly dose of 3HP (12-dose regimen) is recommended for PLHIV on ART that have acceptable drug-drug interactions with Rifapentine such as DTG, EFV and RAL.
- 3HP is NOT recommended for PLHIV on PI or NVP based ART regimen
- In cases where 3HP is contraindicated or cannot be administered, use Isoniazid for 6 months
- Complete necessary recording and reporting tools (TPT register, TPT card, ART care card and register).

Repeat course of TPT is no longer recommended

5.5 Monitoring of PLHIV on TPT

During monthly drug refills, monitor patient for

- Development of active TB (clinical assessment of signs and symptoms of active TB)
- Development of side-effects; e.g., peripheral neuropathy (numbness/tingling sensation of extremities). If present, give Pyridoxine:

- 25mg daily for children
- 50-75 mg daily for adult

- Check for the following symptoms and signs; if present, stop TPT and refer to medical officer for assessment
  - Jaundice
  - Abdominal pain, nausea and vomiting
  - Allergic skin eruptions
- Evaluate adherence and counsel appropriately
- Track any client who misses a scheduled appointment and manage appropriately

Note:

If patient develops symptoms suggestive of active TB during the course of TPT:

- Discontinue TPT
- Evaluate for active TB
- Commence DOTS if confirmed or refer to medical officer.
- Assess for HIV treatment failure

5.6 Management of TPT interruption

For any client who misses an appointment:

- Track the client
- Find out the reason for missed appointment and address as appropriate
- Offer adherence counseling
- Evaluate for active TB
- Make up for the missed doses

For management of TPT interruption refer to Table 25 below

Table 25: Management of interruption of TPT

TPT Regimen	Length of interruption	Next Step
3HR, 6H	Less than 2 weeks	• Resume preventive treatment immediately upon return

		• Add the number of days of missed doses to the total treatment duration.
	More than 2 weeks	a. If treatment interruption occurred after more than 80% of doses expected in the regimen were taken: • No action is required. • Continue and complete the remaining treatment as per original plan. b. If less than 80% of doses expected in the regimen were taken, and the treatment course can still be completed within the expected time for completion, i.e. treatment duration + 33% additional time: • No action is required. • Continue and complete the remaining treatment as per original plan. c. If less than 80% of doses expected in the regimen were taken, and the treatment course cannot be completed within the expected time for completion: • Restart the full TPT course.
3HP	Weekly schedule of one dose missed	**a.** If the missed dose is remembered within the next 2 days: • Take the dose immediately • Continue the schedule as originally planned b. If the missed dose is remembered more than 2 days later: • Take the missed dose immediately and change the schedule for weekly intake to the day the missed dose was taken until treatment completion
	More than 1 weekly doses of 3HP missed	a. If between 1 - 3 weekly doses are missed: • Treatment is continued until all 12 doses are taken, thus prolonging the treatment duration to a maximum of 16 weeks. b. If 4 or more weekly doses are missed, restart the full TPT course.
1HP	Less than 1 week	a. If more than 80% (23) of doses expected in the regimen were taken: • No action is required, complete the remaining doses.

		b. If less than 80% (23) of doses expected in the regimen were taken. • Resume treatment immediately upon return • Add the missed doses to the total treatment duration to complete the course within a maximum of 6 weeks.
	More than 1 week	a. If more than 7 consecutive doses were missed. • Consider restarting the complete course of 1HP regimen. b. If more than 7 doses were missed intermittently. • Resume preventive treatment immediately upon return • Add the missed doses to the total treatment duration to complete the course within a maximum of 8 weeks. **If adherence to 1HP is not possible, consider discontinuing it and offering an alternative daily regimen or 3HP**

Note: If attempt to complete TPT fails after 3 attempts, no further effort should be made

5.7 Outcomes of TB Preventive Treatment

HCW should ensure that all PLHIV started on TPT are evaluated after completing their treatment and assigned a treatment outcome which should be documented in the monitoring tools. The following are the possible treatment outcomes:

1. Completed treatment
2. Loss to follow-up
3. Not evaluated
4. Died
5. Developed active TB

5.8 Contact Investigation and Management

The main purpose of contact investigation and management is two-fold: firstly, to identify all contacts of confirmed TB cases for TB screening and secondly, to identify those who would be eligible for TB preventive therapy (TPT). Refer to the algorithm below for management of HIV negative contacts of bacteriologically positive TB cases

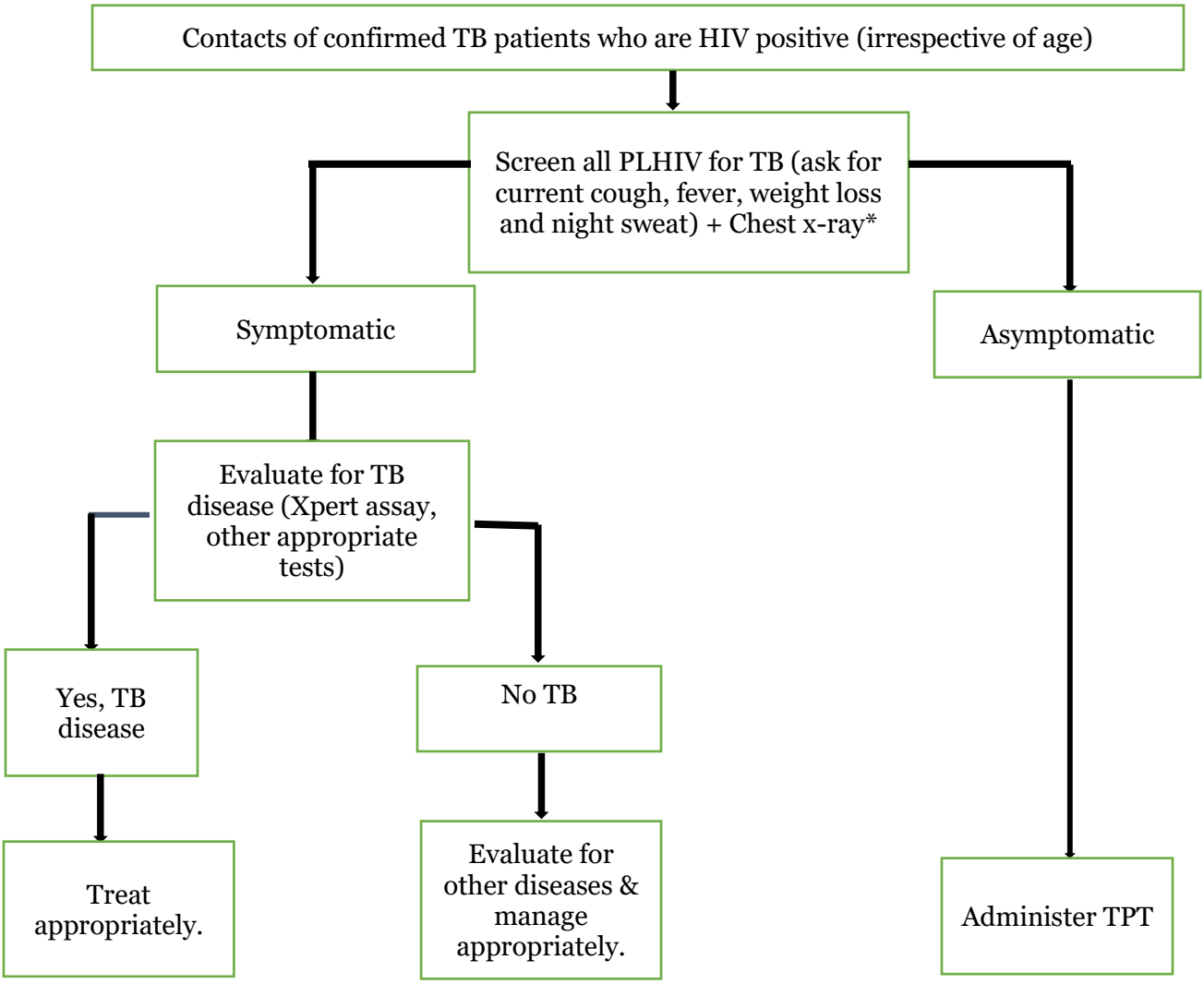


Figure 11: Algorithm for managing PLHIV that are contacts of TB cases

For more details on contact management and TPT, refer to the National TB Guidelines

CHAPTER SIX
Management of other common Opportunistic Infections among PLHIV

6.1 Introduction

Opportunistic infections (OIs) are infections or disease conditions that take advantage of the depressed immunity of HIV-infected persons. TB is the most important OI in terms of morbidity and mortality in PLHIV. There are other OIs of clinical importance and HCW are expected to be familiar with them and be able to give treatment to alleviate the symptoms using the syndromic management approach or refer cases as required.

6.2 Common Opportunistic Infections

The common OIs are due mainly to viral, bacterial, fungal, and parasitic/protozoal organisms.

The table in annex 5 shows some OIs, common symptoms, method of diagnosis and treatment.

6.3 Preventive strategies for other common OIs in PLHIV

There are currently two main strategies for the prevention of OIs; Cotrimoxazole preventive therapy (CPT) - which provides protection to a wide range of bacterial and parasitic infections and tuberculosis preventive therapy (TPT), which is useful for prevention of TB. For TPT, please refer to Chapter 5.

6.3.1 Cotrimoxazole Preventive Therapy (CPT)

Cotrimoxazole preventive therapy (CPT) is the use of cotrimoxazole (CTX) for the prevention of several secondary bacterial, fungal and parasitic infections in PLHIV. It helps to improve the quality of life and reduce the rate of death among PLHIV and those that are co-infected.

When to give CPT in PLHIV

The following are the eligibility criteria for CPT:

- Adults with severe or advanced HIV clinical disease (WHO stage 3 or 4)
- Asymptomatic PLHIV with CD4+ cell count of $\leq 500/mm^3$
- PLHIV with active TB irrespective of CD4+ cell count
- Pregnant PLHIV after the first trimester

- HIV-exposed infants 6 weeks of age
- Children and adolescents with HIV, irrespective of clinical and immunological status.

Priority should be given to all children younger than 5 years old (regardless of clinical or immunological status) and PLHIV with AHD (WHO clinical stage 3 or 4) and/or those with a CD4+ cell count ≤500 cells/mm^3

Starting Patients on CPT
Before commencing a client on CPT, the HCW should:

- Verify HIV status.
- Take medical history and conduct physical examination.
- Counsel on OIs in HIV infection.
- Treat pre existing OIs.
- Screen for contraindications to CPT: e.g., known allergy to Sulphur-containing drugs, first trimester pregnancy, kidney, or liver disease.

In addition, the patient should be counselled for drug adherence and given detailed information of the likely side effects of Cotrimoxazole and action to take in the event of the occurrence of any.
Adverse drug reactions from CTX include skin eruptions, which may be severe (Stevens Johnson syndrome), nephritis, hepatitis, anaemia and hyperkalaemia.

Dosage of Co-trimoxazole for CPT
The table below shows the dose of cotrimoxazole for prophylaxis

Table 26: Dose of Cotrimoxazole Prophylaxis

Adult	Children
≥ 14 years or >30 kg: 960 mg daily	<6 months or < 5 kg: 120mg daily 6 months–5 years or 5-15 kg: 240 mg daily 6–14 years or 15–30 kg: 480 mg daily

Monitoring PLHIV on CPT

- PLHIV should be reviewed monthly initially, and then three - monthly thereafter if the medications are tolerated
- Laboratory monitoring of adults should take place every six months or when clinically indicated. This should include hemoglobin and white cell count

Discontinuing CPT

CPT can be discontinued if side-effects occur.

For patients with contra-indication to CPT,

- In adults, give azithromycin, 1gm weekly or dapsone 100mg daily
- In children, give dapsone 2mg/kg, once daily

CHAPTER SEVEN
Infection Prevention and Control

7.1 Introduction

Infection prevention and control (IPC) practices in healthcare settings are measures for preventing avoidable transmission of infections among patients and HCW. The effectiveness of these practices and measures are largely dependent on consistent implementation at all levels of the health system.

7.2 Standard Infection prevention and control practices

There are minimum infection prevention practices that should be carried out in any health care setting regardless of the infection status. These standard precautions include:

- Hand hygiene.
- Use of personal protective equipment (e.g. gloves, masks, eyewear).
- Cough etiquette.
- Proper disposal of sharps.
- Injection safety.
- Sterile instruments and devices.
- Clean and disinfected environmental surfaces.
- Proper waste management.

The standard precautions should be supplemented in the TB/HIV setting with the transmission-based precautions as outlined below.

7.3 TB Infection prevention and control (TB-IPC) in health care settings

TB is an airborne infection and HCWs, patients as well as other individuals within the health care setting are particularly at risk. Persons who are immuno-suppressed such as PLHIV are at high risk. Long waiting hours, overcrowding and poor ventilation increase the risk of TB transmission.

There are three main control measures to reduce the risk of TB infection.

- Administrative
- Environmental
- Personal protective measures.

7.3.1 Administrative Control Measures

These measures serve as the first and most important level in the hierarchy of prevention of the spread of TB in HIV settings.

The measures can be accomplished through the prompt recognition, separation, service provision, and referral of persons with potentially infectious TB disease (FAST strategy-Finding TB cases Actively, Separating Safely and Treating effectively).

This includes:

- Constitution of an IPC committee.
- Development of facility-specific TB infection control policies/plan.
- Appointment of TB Infection Control Focal Person.
- Ensuring regular TB-IPC meetings.
- Creating awareness on cough etiquette.
- Providing uninterrupted supply of personal protective equipment (PPE) and other infection control materials.
- Establishment of effective waste management systems for IPC.
- Production and dissemination of IPC IEC materials for use in such settings.
- Ensuring respiratory separation / isolation of people with presumed or confirmed TB by dedicated cough/triage officers.
- Prompt initiation of treatment in people with TB disease.

7.3.2 Environmental control measures

The second level of the hierarchy is the use of environmental controls to prevent the spread of TB in HIV care settings. If the work practice controls are inadequate, environmental controls will not eliminate the risk of spread of TB.

Environmental control measures include: Ventilation, upper room germicidal ultraviolet (GUV) systems and safe collection of sputum samples.

Ventilation

Ventilation can be natural or mechanical and involves movement of air in a building and replacement of air in a building with air from outside. When fresh air enters a room, it dilutes the concentration of particles, such as droplet nuclei containing *M. tuberculosis*.

Natural Ventilation

- Open doors and windows allow free movement of air in and out of a room. Waiting areas and examination rooms should be designed to have maximum natural ventilation.

Mechanical ventilation

- Use of fans.
- Recirculated air through high-efficiency particulate air [HEPA] filters.
- Use of air extractors.
- Use of whirly bird.

Ultraviolet germicidal irradiation (UGI)

This should be considered where resources and expertise allow. The two most important forms are Upper room irradiation and duct irradiation.

Safe collection of sputum samples for TB diagnosis

Always collect sputum samples for TB diagnosis outside (an open environment) and away from other people not in small rooms such as toilets or other enclosed areas.

7.3.3. Personal protective measures

The third level of the hierarchy is the use of personal protective measures. Personal protective measures can offer protection only if appropriate work practice and environmental controls are in place.

Personal protective measures include:

- Ensuring the correct, consistent and complete use of standardized, recommended protective equipment.
- Encouraging the appropriate use of N95 respirators, surgical face masks, handkerchiefs or tissue paper while coughing. In the absence of these, the elbow can be used to cover the mouth.

- Ensuring hand hygiene at all time.
- Use of other forms of personal protective equipment (PPE) such as goggles, coats, face shield where indicated.

7.4 Prevention of HIV transmission in health care settings

To prevent HIV transmission in health care settings, standard precautions should always be practiced.

The following are recommended precautions for HCWs

- Assume that all blood and body fluids are potentially infectious.
- Handle all "sharps" (needles and syringes) carefully and discard used ones into a disposable container, then burn them.

The table below gives some guidance on precautions against risk of HIV transmission in health care settings.

Table 27: Precautions to take in health care settings

Exposure to risk	Precaution for prevention of transmission of HIV
Venepuncture	• Wear gloves • Use a closed vacuum system if available • Discard needle and syringe into sharps box • Discard gloves and swabs into leak-proof plastic bag for incineration (burning) • Label blood bottle and request form
Invasive procedure, surgery or delivery of a baby	• Wear gloves and apron • Protect your eyes (glasses or protective goggles) • Discard sharps into sharps box
Spilled blood	• Clean up immediately using available disinfectant (e.g., Dettol, Purit, Savlon, Izal)
Resuscitation	• Avoid mouth-to-mouth resuscitation (use Ambu-bag)

Actions recommended following a needle-stick injury or mucosal exposure

In the event of an injury with a sharp object such as a needle or scalpel that has been used on a patient or a mucous surface being contaminated with blood or secretions, follow the steps below:

- Do not squeeze or rub the injury site.
- Allow blood or secretion to flow freely.
- Wash exposed area immediately with soap and running water or antiseptic solutions such as 2% polyhexidine or 70% glutaraldehyde.
- After a splash to the eye or any other mucous surface, irrigate/rinse the exposed area immediately with water (preferably running water) or normal saline.
- Report the exposure to a senior member of staff, supervisor or the PEP officer.
- If eligible, refer for ARV prophylaxis.

For more details refer to the National Guideline for HIV Prevention, Treatment and Care.

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Annex 1: WHO clinical staging of HIV disease in adults, adolescents and children

Adults and adolescents[a]	Children
Clinical Stage 1	
• Asymptomatic • Persistent generalized lymphadenopathy	• Asymptomatic • Persistent generalized lymphadenopathy
Clinical Stage 2	
• Moderate unexplained weight loss (<10% of presumed or measured body weight) • Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis) • Herpes zoster • Angular cheilitis • Recurrent oral ulceration • Papular pruritic eruption • Fungal nail infections • Seborrhoeic dermatitis	• Unexplained persistent hepatosplenomegaly • Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis) • Herpes zoster • Lineal gingival erythema • Recurrent oral ulceration • Papular pruritic eruption • Fungal nail infections • Extensive wart virus infection • Extensive molluscum contagiosum • Unexplained persistent parotid enlargement
Clinical Stage 3	
• Unexplained severe weight loss (>10% of presumed or measured body weight) • Unexplained chronic diarrhoea for longer than 1 month • Unexplained persistent fever (intermittent or constant for longer than 1 month) • Persistent oral candidiasis • Oral hairy leukoplakia • Pulmonary tuberculosis • Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)	• Unexplained moderate malnutrition[b] not adequately responding to standard therapy • Unexplained persistent diarrhoea (14 days or more) • Unexplained persistent fever (above 37.5°C, intermittentor constant, for longer than one 1 month) • Persistent oral candidiasis (after first 6 weeks of life) • Oral hairy leukoplakia • Lymph node tuberculosis • Pulmonary tuberculosis • Severe recurrent bacterial pneumonia • Acute necrotizing ulcerative gingivitis or periodontitis • Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 x 10^9/l) or

• Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis • Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 x 10^9/l) and/or chronic thrombocytopaenia (<50 x 10^9/l)	chronic thrombocytopaenia (<50 x 10^9/l) • Symptomatic lymphoid interstitial pneumonitis • Chronic HIV-associated lung disease, including bronchiectasis
Clinical stage 4[c]	
• HIV wasting syndrome • Pneumocystis (jirovecii) pneumonia • Recurrent severe bacterial pneumonia • Chronic herpes simplex infection (orolabial, genital or anorectal of more than 1 month's duration or visceral at any site) • Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) • Extrapulmonary tuberculosis • Kaposi sarcoma • Cytomegalovirus infection (retinitis or infection of other organs) • Central nervous system toxoplasmosis • HIV encephalopathy • Extrapulmonary cryptococcosis, including meningitis • Disseminated nontuberculous mycobacterial infection • Progressive multifocal leukoencephalopathy • Chronic cryptosporidiosis • Chronic isosporiasis • Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis)	• Unexplained severe wasting, stunting or severe malnutrition[d] not responding to standard therapy • Pneumocystis (jirovecii) pneumonia • Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia) • Chronic herpes simplex infection (orolabial or cutaneous of more than 1 month's duration or visceral at any site) • Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) • Extrapulmonary tuberculosis • Kaposi sarcoma • Cytomegalovirus infection (retinitis or infection of other organs with onset at age more than 1 month) • Central nervous system toxoplasmosis (after the neonatal period) • HIV encephalopathy • Extrapulmonary cryptococcosis, including meningitis • Disseminated nontuberculous mycobacterial infection • Progressive multifocal leukoencephalopathy • Chronic cryptosporidiosis (with diarrhoea) • Chronic isosporiasis

• Lymphoma (cerebral or B-cell non-Hodgkin) • Symptomatic HIV-associated nephropathy or cardiomyopathy • Recurrent septicaemia (including nontyphoidal Salmonella) • Invasive cervical carcinoma • Atypical disseminated leishmaniasis	• Disseminated endemic mycosis (extrapulmonary, histoplasmosis, coccidioidomycosis, penicilliosis) • Cerebral or B-cell non-Hodgkin lymphoma • HIV-associated nephropathy or cardiomyopathy

a. *In the development of this table, adolescents were defined as 15 years or older. For those aged less than 15 years, the clinical staging for children should be used.*
b. *For children younger than 5 years, moderate malnutrition is defined as weight-for-height <–2 z-score or mid-upper arm circumference ≥115 mm to <125 mm.*
c. *Some additional specific conditions can be included in regional classifications, such as penicilliosis in Asia, HIV-associated rectovaginal fistula in southern Africa and reactivation of trypanosomiasis in Latin America.*
d. *For children younger than 5 years of age, severe wasting is defined as weight-for-height <–3 z-score; stunting is defined as length-for-age/height-for-age <–2 z-score; and severe acute malnutrition is either weight for height <–3 z-score or mid-upper arm circumference <115 mm or the presence of oedema.*

Annex 2: SOP for Rifabutin Use in HIV/TB Co-Infected Patients Requiring Protease Inhibitor-Based Antiretroviral Therapy

Introduction

Use of rifampicin with standard doses of protease inhibitors (PI) is not recommended due to a significant reduction in blood levels of PIs, risking virologic failure. Although adjusted doses of lopinavir/ritonavir may overcome this interaction.

Therefore, rifabutin is preferred to rifampicin in TB/HIV co-infected patients requiring PI-based antiretroviral therapy (ART). Rifabutin has comparable efficacy to rifampicin and is well-tolerated but does not significantly reduce the blood levels of ritonavir-boosted PIs. However, the ritonavir-boosted PI significantly increases blood levels of rifabutin; therefore, when co-administered, rifabutin must be given at a lower than standard dose.

Based on the available evidence to-date, the recommended rifabutin dose in adults when given in combination with ritonavir-boosted PIs is 150 mg every day (instead of standard doses of 300 mg once daily). PI dose adjustments are not required when given with rifabutin.

Rifabutin should only be used among PLHIV who require PI-based ARV and anti-TB drugs

1. Drug Tables:

1.1. ADULTS

Regimen 1: Regimen and dosages for Adult with susceptible PTB/EPTB cases* (6months regimen): 2RfbHZE/ 4RfbH

Regimen	Pre-treatment weight		
*Intensive phase: daily **supervised** for 2 months*	*> 55 kg*	*40 – 55 kg*	*21-39 kg*
(Rfb) Rifabutin 150 mg **Daily**	1	1	1
Combined tablet of EH (400mg + 150mg) **Daily**	2	2	1
(Z) Pyrazinamide 400 mg **Daily**	4	3	2
Continuation phase: **daily** supervised **RfbH** *for 4 months*			
(Rfb) Rifabutin 150mg **Daily**	1	1	1
(H) Isoniazid 100mg **Daily**	3	3	2

Refers to all PTB and EPTB cases with the exception of TB meningitis & TB of bones/joints

Regimen 2: Regimen and dosages for adults with TB meningitis and Osteo-articular TB (12months regimen): 2SRfbHZE/10(RfbHE)

Regimen	Pre-treatment weight		
*Intensive phase: daily **supervised** for 2 months*	*> 55 kg*	*40 – 55 kg*	*21-39 kg*
(Rfb) Rifabutin 150 mg **Daily**	1	1	1

Combined tablet of EH (400mg + 150mg) **Daily** (Z) Pyrazinamide 400 mg **Daily**	2 4	2 3	1 2
Continuation phase: **daily** supervised **RfbH** *for 10 months* (Rfb) Rifabutin 150mg **Daily** (H) Isoniazid 100mg **Daily**	1 3	1 3	1 2

Use of rifabutin in TB/HIV co-infected pregnant women on PI-based ARVs:
For pregnant women requiring the use of ritonavir-boosted PI-based ART or PMTCT and anti-TB therapy, change rifampicin to rifabutin. Dosing of rifabutin during pregnancy should follow the recommendations outlined above.

1.2. CHILDREN (0-14 YEARS)

Regimen I: Regimen and dosages for children with susceptible PTB/EPTB cases*(2RfbHZ+E/4RfbH)

Regimen	**Pre-treatment weight**		
*Intensive phase: daily **supervised** for 2 months*	*15-20 kg*	*8-14 kg*	*5-7 kg*
(H) Isoniazid 100 mg	2	1	1
(Rfb) Rifabutin* daily			

(Z) Pyrazinamide 400 mg	1	1	½
(E) Ethambutol 100mg	3	2	1
Continuation phase: daily supervised for 4 months			
(Rfb) Rifabutin* daily			
(H) Isoniazid 100 mg	2	1	1

Refers to all PTB and EPTB cases with the exception of TB meningitis & TB of bones/joints

Regimen 2: Regimen and dosages for children with TB meningitis and Osteo-articular TB (12 months' regimen): 2SRfbHZE/10(RfbHE)

Regimen	**Pre-treatment weight**		
*Intensive phase: daily **supervised** for 2 months*	*15-20 kg*	*8-14 kg*	*5-7 kg*
(H) Isoniazid 100 mg	2	1	1
(Rfb) Rifabutin* daily	1	1	½
(Z) Pyrazinamide 400 mg	3	2	1
(E) Ethambutol 100mg			
Continuation phase: daily supervised for 10 months			
(Rfb) Rifabutin* daily			

(I) Isoniazid 100 mg	2	1	1

Rifabutin dosage in children

- Children < 1 year:
  10 mg/kg body weight given **daily**

- Children > 1 year:
  5-10 mg/kg body weight given **daily**

* Rifabutin (Rfb) is available in capsule form and has to be compounded when required in children, usually by a pharmacist in a specialized centre.

2. Adverse Events/Toxicity of Rifabutin

- Abdominal pain
- Bloating
- Chest pain
- Taste perversion
- Headache
- Discolouration of body fluids, giving a red-orange or red-brown colour to urine, faeces, saliva, skin, sweat, and tears
- Allergic reactions, including skin rash and itching
- GI effects, including anorexia, diarrhoea, dyspepsia, nausea, and vomiting
- Haematologic abnormalities, including anaemia, leukopenia, neutropenia, and thrombocytopenia.
- Uveitis – characterized by itching, decreased vision, photophobia, pain, and temporary blindness in some patients. Patients with uveitis should be referred to ophthalmologist

Among this group of patients on ARVs and Rifabutin containing anti-TB drugs, the side effects may be similar or may potentiate each other. Therefore, when side effects occur, refer the patient to a Medical officer.

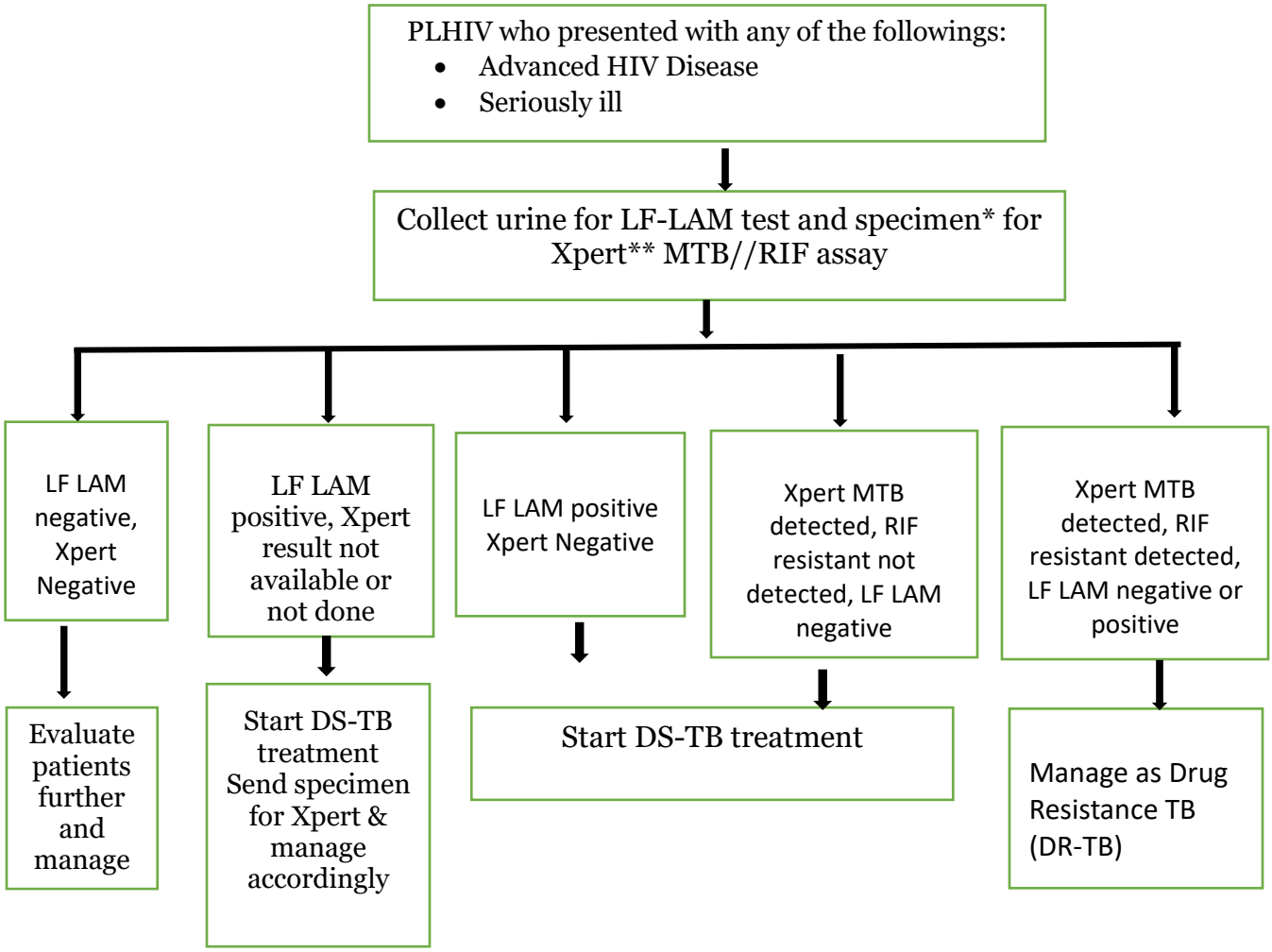
Note:

Rifabutin decrease the efficacy of oral contraceptives that contain estrogen by inducing the hepatic metabolism of estrogen. Patients using oral contraceptives should consider changing to nonhormonal methods of birth control.

Rifabutin is metabolized through CYP3A enzymes, inhibitors of these enzymes, such as fluconazole or clarithromycin, may increase rifabutin plasma concentrations. The dosage of rifabutin may need to be reduced.

In cases of severe renal impairment (creatinine clearance less than 30 mil/min), the dosage of rifabutin may also need to be reduced.

Annex 3: Algorithm for LF-LAM and Xpert MTB/RIF assay in PLHIV



* Where sputum is not available, stool or other specimens may be used as appropriate

** Where Xpert test is not available, Truenat MTB-RIF Dx test may be used

Annex 4: Weight-based dosing for ARV formulations for infants and children:

Dolutegravir:

WHO welcomes the recent decision by the U.S. Food and Drug Administration (FDA) to approve a dispersible 5 mg formulation of dolutegravir (DTG) for use in infants and children living with human immunodeficiency virus type 1 (HIV1). The tablet, taken orally, has been approved for use in paediatric patients from four weeks of age weighing at least 3 kg in combination with other antiretroviral treatments.

Dolutegravir dispersible tablets:

DTG dispersible tablets are approved by the FDA for use in paediatric patients who are treatment naive or treatment-experienced but naive to integrase strand transfer inhibitor (INSTI) treatment:

Paediatric Body Weight	Recommended Dose of Dolutegravir Dispersible Tablets	Number of 5mg tablets
3 kg to <6 kg	5 mg once daily	1
6 kg to <10 kg	15 mg once daily	3
10 kg to <14 kg	20 mg once daily	4
14 kg to <20 kg	25 mg once daily	5
≥20 kg	30 mg once daily	6

Dolutegravir film-coated tablets:

For use in patients who are treatment-naive or treatment-experienced but naive to INSTI treatment.

Do not use DTG film-coated tablets in patients weighing <14 kg.

DTG film-coated tablets and DTG dispersible tablets are not bioequivalent and are not interchangeable on a milligram-per-milligram basis. Each formulation has different doses.

Dosing of film-coated tablets for paediatric patients weighing ≥14 kg who can swallow tablets:

Paediatric Body Weight	**Recommended Dose[a] of Dolutegravir Film-coated Tablets**	**Number of 5mg tablets**
14 kg to <20 kg	40 mg once daily	4 x 10 mg
≥20 kg	50 mg once daily	1 x 50 mg

Drug-dosing of liquid formulations in infants less than 4 weeks of age:

Drug	**Strength of oral liquid**	**2-3 kg**		**3-4 kg**		**4-5 kg**	
		AM	PM	AM	PM	AM	PM
LPV/r	80/20 mg/mL	0.6 mL	0.6 mL	0.8 mL	0.8 mL	1 mL	1 mL
	Granules 40 mg/10 mg sachet	–	–	2	2	2	2

RAL	10 mg/mL (Oral granules for suspension: 100 mg/sachet)	<1 week	0.4 mL (once daily)[C]		0.5 mL (once daily)		0.7 mL (once daily)	
		>1 week	0.8 mL	0.8 mL	1 mL	1 mL	1.5 mL	1.5 mL

Simplified dosing of child-friendly solid formulations for once-daily dosing in infants and children 4 weeks of age and older:

Drug	Strength of paediatric tablet	Number of tablets or capsules by weight band once daily					Strength of adult tablet	Number of tablets or capsules by weight band once daily
		3–5.9 kg	6–9.9 kg	10–13.9 kg	14–19.9 kg	20–24.9		25–34.9 kg

						kg		
ATV	Capsules 100 mg	–	–	2	2	2	300 mg	1
	Capsules 200 mg	–	–	1	1	1		
DRV	Tablet 600 mg	–	–	–	1	1	600 mg	1
	Tablet 150 mg	–	–	–	4	4		
RTV	Tablet 25 mg	–	–	–	4	4	100 mg	1
	Tablet 50 mg	–	–	–	2	2		
DTG	Film-coated Tablet 50 mg	–	–	–	–	1	50 mg	1

Simplified dosing of child-friendly solid and oral liquid formulations for twice-daily dosing in infants and children 4 weeks of ae and older:

Drug	Strength of paedaitric tablets or	Number of tablets or MLS by weight-band morning (AM) and evening(PM)	Strength of adult tablet	Number of tablets by weight

	oral liquid											band	
		3–5.9 kg		6–9.9 kg		10–13.9 kg		14–19.9 kg		20–24.9 kg		25–34.9 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
Solid formulations													
LPV/r	Tablet 100 mg/25 mg	–	–	–	–	2	1	2	2	2	2	–	3	3
	Pellets 40 mg/10 mg	2	2	3	3	4	4	5	5	6	6	–	–	–
	Granules 40 mg/10 mg sachet	2	2	3	3	4	4	5	5	6	6	–	–	–
	80/20 mg/ml	1 ml	1 ml	1.5 ml	1.5 ml	2 ml	2 ml	2.5 ml	2.5 ml	3 ml	3 ml	–	–	–
DRV	Tablet 75 mg	–	–	–	–	–	–	5	5	5	5	400 mg	1	1
	100 mg/ml	–	–	–	–	2.5 ml	2.5 ml	3.5 ml	3.5 ml	–	–	–	–	–
RTV	Tablet 25 mg	–	–	–	–	–	–	2	2	2	2	100 mg	1	1
	Tablet 50 mg	–	–	–	–	–	–	1	1	1	1			
	80 mg/ml	–	–	–	–	0.5 ml	0.5 ml	0.6 ml	0.6 ml	–	–	–	–	–
RAL	Chewable tablets 25 mg	1	1	2	2	3	3	4	4	6	6	400 mg	1	1
	Chewable tablets 100 mg	–	–	–	–	–	–	1	1	1.5	1.5			
	10 mg/mL (Oral granules	3 m	3 mL	5 mL	5 mL	8 mL	8 mL	10 mL	10 mL	–	–			

	for suspension: 100 mg/sachet)	L												

Dosing of RTV super-boosting of LPV/r for children receiving rifampicin containing TB treatment:

Drug	Strength of paediatric tablets or oral liquid	Number of tablets or MLS by weight-band morning (AM) and evening (PM)										Strength of adult tablet	Number of tablets by weight band	
		3–5.9 kg		6–9.9 kg		10–13.9 kg		14–19.9 kg		20–24.9 kg			25–34.9 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
For children able to swallow tablets														
LPV/r	Tablet 100/25 mg	–	–	–	–	2	1	2	2	2	2	100/25 mg	3	3
RTV	Tablet 100 mg	–	–	–	–	1	1	1	2	1	2			
	Tablet 50 mg	–	–	–	–	2	2	3	3	3	3	100 mg	2	2
	Tablet 25 mg	–	–	–	–	4	4	6	6	6	6			
For children unable to swallow tablets														
LPV/r	Oral solution[c] 80/20 mg/ml	1 ml	1 ml	1.5 ml	1.5 ml	2 ml	2 ml	2.5 ml	2.5 ml	3 ml	3 ml	-	-	-
	Pellets[d] 40 mg/10 mg	2	2	3	3	4	4	5	5	6	6	-	-	-
	Granules 40 mg/10 mg sachet	2	2	3	3	4	4	5	5	6	6	-	-	-
RTV	Oral solution 80 mg/ml	0.8 ml	0.8 ml	1.2 ml	1.2 ml	1.5 ml	1.5 ml	2 ml	2 ml	2.3 ml	2.3 ml	-	-	-
	Powder 100 mg/packet	-	-	1	1	1	1	1	2	1	2	-	-	-

Annex 5: Common opportunistic infections and their management

Infection/ Conditions	Causative organisms	Symptoms and signs	Diagnosis	Treatment and Prophylaxis	Comments
MULTIPLE CAUSATIVE ORGANISMS					
Acute watery Diarrhoea	**Viruses:** -*Rotavirus* -*Enteroviruses* **Bacteria:** -Enterobacteriae -E. Coli -C. jejuni	Frequent watery stools	Clinical Laboratory: - Stool m/c/s Serology	Rehydrate (SSS, ORS or Resomal as required) Zinc supplement 20mg daily for 10-14 days for paediatric patients	Provide and maintain adequate nutrition E,U,Cr is useful to monitor renal complications
Dysentery	-*E. hystolitica* -*G. Lamblia* -*Isospora belli* -*Cryptosporidia* -*Salmonella spp.* *Shigella* -*C. jejuni* *Cyclospora*	Frequent watery stools, abdominal cramps bloody stools, fever, nausea and vomiting, dehydration	Clinical Laboratory: -Stool m/c/s Serology, e.g., Widal test	Oral rehydration If antibiotics required: -Ciprofloxacin -Metronidazole and CTX For Strongyloidiasis: - Albendazole Oral Zinc therapy	Provide and maintain adequate nutrition E, U. Creatinine is useful to monitor renal complications

	-*Microsporidia* -*C. albicans* -*M. avium complex* -*S. Stercoralis* *Clostridium deficile*				
Pneumonia	Respiratory viruses			Viral pneumonia is self-limiting – requires only supportive care	

	Bacteria: *S. pneumoniae* *H. influenza* *S. aureus* *M. catarhalis* *Kl. pneumonia* *P. aeruginosa*	Fever, chills, cough and pleuritic chest pain, difficulty/ fast breathing. Crepitations, bronchial breath sounds	Clinical Laboratory: blood culture. Chest x-ray -sputum examination	Bacterial: -Out-patient therapy with CTX or Amoxicillin or Amoxicillin/clavulanic acid. For in-patient therapy: -2nd and 3rd generation cephalosporin as 2nd line. o (Azithromycin or clarithromycin). Respiratory quinolones (levofloxacin) in adults.	- For severe pneumonia in children <12 months old treat PJP presumptively with CTX. - If facilities to exclude PJP infections are not available or if a child on CPT develops bacterial pneumonia do not treat with CTX but refer. - Quinolones are a 2nd line anti TB drug hence rule out TB before using quinolones(levofloxacin)

	Fungal: *Pneumocystis jiroveci*	Acute/subacute non-productive cough, difficulty in breathing, SPO2 <92% at rest on room air	Bronchoalveolar lavage, induced and expectorated sputum, nasopharyngeal aspirate and oral washing. Giemsa statin can be used for identification.	• For Moderate to severe PJP: IV Cotrimoxazole (TMP 15– 20 mg and SMX 75– 100 mg)/ kg/ day given qds or tds (switch to PO after clinical improvement for 21 days). •For Mild PJP: Cotrimoxazole: (TMP 15– 20 mg/ kg/ day and SMX 75– 100 mg/ kg/ day), given PO in 3 divided doses for 21 days Alternative: • Moderate to Severe PJP: Primaquine 30 mg (base) PO once daily + clindamycin [IV 600 qds or 900 mg tds] or [PO 300 mg q6h or 450 mg q8h], Or Pentamidine 4 mg/ kg IV once daily infused over at least 60	-

				minutes, may reduce the dose to 3 mg/ kg IV once daily because of toxicities • For Mild PJP: Dapsone 100 mg PO daily + TMP 15 mg/ kg/ day PO (3 divided doses), OR Primaquine 30 mg (base) PO daily + clindamycin PO (300 mg q6h or 450 mg q8h)	

Acute Pharyngo–tonsillitis	Respiratory viruses Bacteria: - *Strep. pneumoniae* - *H. influenza* - *Moxerella Catarhalis* *Klebs. Pneumoniae*	Fever, cough, vomiting, refusal of feeds, drooling of saliva, inflamed tonsils/ pharynx.	Clinical Laboratory: Throat swab for m/c/s	Amoxicillin or Amoxicillin/ clavulanic acid. 2nd generation cephalosporin 3rd and 4th generation cephalosporin, and respiratory quinolones (levofloxacin)	
Acute otitis media	Respiratory viruses Bacteria: - *Strep. pneumoniae* - *H. influenza* - *Staph. Aureus* - *Moraxella catarhalis* *Klebs. Pneumoniae*	Fever, vomiting, cough, ear-tugging; Hyperaemic tympanic membrane, purulent ear discharge	Clinical Laboratory: Ear swab for m/c/s	Amoxicillin or Amoxicillin/ clavulanic acid 2nd generation cephalosporin 3rd and 4th generation cephalosporin, and respiratory quinolones (levofloxacin)	

VIRAL					
Hepatitis	Hepatitis B Virus	There may be no signs and symptoms except as in chronic liver disease.	Screen for HBsAg. If positive, screen for the following; 1. HBsAg 2. Anti HBeAg 3. Anti HBcAg 4. Anti HCV 5. HBV-DNA 6. LFT 7. Abdominal ultrasound	The regimen should include TDF and 3TC, and where TDF is contraindicated, substitute for TDF and add Entecavir	1. HBsAg quantification if available 2. Liver biopsy if necessary 3. Baseline alpha feto-protein (AFP) if possible Refer for specialist care if complicated. Some may require Peg-Interferon treatment Baseline AFP if possible
	Hepatitis C Virus	There may be no signs and symptoms except as in chronic liver disease.	1. Anti HCV 2. LFT 3. Abdominal ultrasound. 4. HCV RNA (Refer if positive) 5. FBC	Direct-acting antiviral (DAA); The Guideline Recommends the pangenotypic regimen consisting of Sofosbuvir-Daclatasvir **Refer for specialist care for complicated cases.**	

Herpes zoster (Shingles)	*Varicella zoster virus*	Painful vesicular lesions in a dermatomal distribution, on face and trunk	Clinical	**Adult:** Acyclovir: 800mg 5 times/day for 7 days + amitriptyline 25mg nocte OR - 10 mg/kg IV q8hr for 7 days - Analgesics – NSAIDS, carbamazepine, amitriptyline - Local application of calamine lotion; - Topical application of Acyclovir cream - For painful vesicular unilateral lesions on face or trunk. - Add gentian violet topical application, tab pregabalin 75mg BD (adult) 7 to 10 days,	Refer intractable cases for specialist care. Refer cases of herpes zoster involving the eye and ear for specialist care.

				Paediatrics: Tab Acyclovir 30mg/kg/day tds x 7 days	
Herpes simplex	Herpes simplex virus (HSV) 1 and 2	Blisters or painful sores on or around the affected area like the skin, mouth, genitals and rectum.	Clinical	Acyclovir Tab 400mg tds for 7 – 14 days OR 200mg 5 times daily for 7 -14 days	
		Herpes Simplex can present with Fever, altered consciousness, convulsions ± focal neurological signs	Increased CSF: serum HSV antibody ratio CT Scan, Viral isolation,	IV Acyclovir Paediatrics: 20mg/kg tid x 21days Adult: 10-15 mg/kg IV q8hr for 14-21 days	Nausea, vomiting, diarrhoea, headache, malaise, rash, seizures, renal dysfunction
Cytomegalovirus: Oesophagitis Enteritis Colitis Retinitis CNS involvement	Cytomegalovirus (CMV)	Enterocolitis: Fever, cramps, dysphagia, odynophagia, diarrhoea ± blood; CNS: Delirium, lethargy, headache, malaise disorientation, neck stiffness, cranial nerve palsy	Clinical. <u>Laboratory:</u> Biopsy (intracellular inclusions) Serology Skull X-ray CT Scan CMV in CSF	Ganciclovir 5mg/kg IV bid x 2-3 weeks; Foscarnet IV 40-60mg/kg 8 hrly x 2-3 weeks	

		Retinitis: photophobia, blurred vision or "floaters"	Retinitis – Ophthalmological examination		
Measles	*Measles virus*	Fever, cough, red eyes, kerato-conjunctivitis, coryza, maculo-papular rash; Complications: Pneumonia, diarrhoeal disease, malnutrition.	Clinical	Supportive therapy Antipyretics Vitamin A, antibiotics as indicated, adequate hydration	Highly contagious; Refer Complications; Nutrition support
Chicken pox	*Varicella virus*	Fever, centrifugal umbilicated rash in crops (starts from trunk to extremities)	Clinical	Supportive therapy Reduce fever with antipyretics Antibiotics for bacterial super-infections	
Anal/Genital warts Cutaneous warts (*Verruca plana)*	*Human papilloma virus*	<u>Anal/Genital:</u> Crops of papules or nodules with a rough surface <u>Verruca plana:</u> Widespread flat hypo/hyper-pigmented rash on face, trunk and	Clinical In addition, laboratory diagnosis with PCR e.g., Xpert HPV tests.	Apply Salicylic acid preparation, or Liquid nitrogen, Cryotherapy or Electrocautery	

		limbs, not itchy, dry, often scaly		Add podophyllin and podophyllotoxin and imiquimod.	
Molluscum contagiosum	Pox virus	Light-coloured nodules with central umbilication commonly seen on face and trunk	Clinical	Leave alone unless super-infected, OR Use Electro-cautery, OR Use of Liquid nitrogen application. Strongly consider cryptococcal skin infection if there are constitutional symptoms. Add Gentian Violet daily application until the lesions resolve.	Antibiotics for bacterial super-infection
Lymphoid interstitial pneumonitis (LIP)	*Unknown, but associated with co-infection with Epstein Barr Virus*	May initially be asymptomatic. Recurrent Cough, respiratory distress, parotid enlargement, generalized	Clinical Diagnosis of exclusion. Chest X-Ray: reticulo-nodular infiltrates, bilateral	Steroids (prednisolone 2mg/kg/day x 6 weeks, taper off) Oxygen Bronchodilators (salbutamol)	Complications of therapy with prednisolone include Hypertension, gastritis, adrenal insufficiency, seizures, pseudo-tumour cerebri, hypokalaemia, fluid retention, glucose intolerance.

		lymphadenopathy, hepatosplenomegaly, digital clubbing, and poor response to TB therapy.	hilar/mediastinal lymphadenopathy;	Chest physiotherapy Referral to a specialist (paediatric pulmonologist)	
BACTERIAL					
Chronic suppurative otitis media	-*S. pneumoniae* -*H. influenza* -*S. Aureus* -*M. Catarhalis* -*Kl. pneumoniae* -*P. aeruginosa*	Ear discharge lasting >14 days	Clinical Laboratory: - Ear swab for m/c/s X-ray of mastoid	Refer to ENT specialist	Hearing loss is a complication
Impetigo	-*Streptococcus spp,* -*Staph. Aureus*	Skin pustules crusts Fever rarely	Clinical	Clean sore with antiseptics Drain pus if fluctuant Ampicillin/cloxacillin Cefuroxime, cefixime, amoxicillin-clavulanic acid and flucloxacillin.	

				Topical agents such as Mupirocin or Retapamulin.	
Sepsis	-*S. pneumoniae* -*H. influenzae* -*Salmonella* -*N. meningitides* -*Staph aureus* -*Gram-negatives (e.g. E. coli)* -*Anaerobes*	Fever Shock	Clinical assessment Laboratory: - FBC - Blood culture - Urine culture - Organ-specific signs/focus of infection determines the needed test(s).	While awaiting m/c/s results, either: -Penicillin + Gentamycin -Amoxicillin/clavulanic acid + genticin -Metronidazole for anaerobes 2nd or 3rd generation cephalosporin and amoxicillin-clavulanic acid with/out other antibiotics depending on the focus of infection.	Refer to a tertiary facility if necessary If in shock, provide supportive therapy
Acute bacterial Meningitis	-*S. pneumoniae* -*H. influenzae* -*Salmonella* -*N. meningitides*	Fever, headache, vomiting, irritability, altered sensorium, convulsions	Clinical assessment Laboratory: -FBC -Blood culture CSF analysis	Penicillin & Chloramphenicol or 3rd generation cephalosporin + Gentamycin Supportive treatment	Refer to a tertiary facility if necessary

	-*Staph aureus*	Nuchal rigidity, bulging fontanelle (in children)			
Mycobacterium Avium Complex	-*M. Avium spp.*	Disseminated form – recurrent fever, chronic diarrhoea, lymphadenopathy, weight loss/failure to thrive, abdominal pain, Respiratory symptoms may occur	Clinical Laboratory: Multiple blood cultures; Lymph node biopsy for intracellular inclusions	Adult: -Clarithromycin 500 mg b.d. + ethambutol 15 mg/kg daily with or without rifabutin (300 mg daily). -Azithromycin (500-600 mg daily) can be substituted for clarithromycin. Paediatrics: -Clarithromycin 7.5mg/kg/dose b.d or azithromycin 5-20mg/kg/dose once daily plus Ethambutol 15mg/kg/day for 6 months. Prophylaxis: guided by CD4+ count	Nausea and vomiting Optic neuritis may occur with ethambutol
FUNGAL					

Candidiasis	*Candidia albicans*	Retrosternal chest pain (heartburn), pain or discomfort on swallowing and features of candidiasis (pseudo membranous, erythematous lesions and angular cheilitis) in the mouth or throat.	- Laboratory: Wet mount microscopy using KOH preparation - Endoscopy should be conducted if no response to antifungal therapy	Adult: Fluconazole – oral 200mg on day 1, then 100 mg daily; doses up to 400 mg/day may be used based on patient's response. Treat for a minimum of 3 weeks and at least 2 weeks after resolution of symptoms or Itraconazole – oral 200mg daily for at least 2 weeks after resolution of symptoms or Oral Nystatin 400,000 – 600,000 IU four times daily for at least 2 weeks after resolution of symptoms. Paediatric:	

				Fluconazole – oral, 6mg/kg stat on day 1, then 3mg/kg/day for 14-21 days. or Oral Nystatin 100,000 – 200,000 IU qds for at least 2 weeks after resolution of symptoms	
Tinea corporis Tinea capitis	*Malassaezia furfur* *Trichophyton rubrum*	Itchy circular lesions with raised edges, fine scaly area in the centre, loss of hair	Clinical • Laboratory: skin scrapings stained with KOH	Topical application: -Whitfield's ointment applied b.d. for 3-5 weeks - 2% Miconazole cream b.d to the skin for 3-5 weeks **Oral therapy: itraconazole/ fluconazole**	Extra caution for possible NVP interactions with ketoconazole (see the section on drug interactions) Internationally ketoconazole relatively contraindicated since 2013 due to increased idiosyncratic reactions

Seborrhoeic dermatitis	• Allergic reaction to yeast infection *(Pityrosporum)*	Greasy scales over scalp and redness of cheek and flexural aspects	• Clinical	Selenium sulphide shampoo, or Tar shampoo followed by sulphur salicylic acid cream or 1% hydrocortisone, or Ketoconazole cream.	Secondary bacterial infection may be common.
PROTOZOA AND PARASITE					
Cryptococcosis	Cryptococcus neoformans	Brain, lung and skin are sites of predilection. CNS: Most frequent – Meningoencephalitis presenting as headache, fever, and later altered mental status as well as meningeal signs	Cryptococcal antigen (CrAg) screening using blood or CSF	Treatment – Amphotericin B and flucytosine and fluconazole. Refer to National HIV treatment guidelines for details of treatment and propylaxis	

Histoplasmosis	Histoplasma spp.	Symptoms are non-specific mimicking TB (pulmonary or extrapulmonary)	Histoplasma urinary antigen screening Tissue diagnosis will require histology of representative sample	- Liposomal amphotericin B (3.0 – 5.0 mg/kg daily intravenously for 1 - 2 weeks) followed by itraconazole (200mg 3 times daily for 3 days and then 200mg twice daily, for a total of 12 weeks) is the preferred therapy for disseminated Histoplasmosis - For mild to moderate disease, itraconazole (200mg 3 times daily for 3 days and then twice daily for at least 12 months is recommended).	

Malaria	-*Mainly P. falciparum*	Fever, chills and rigour, headache, nausea and vomiting	Clinical Laboratory: malaria parasite in blood film RDT.	Uncomplicated: Artemisinin-based Combination Therapy Complicated: • Injectable Artesunate - Avoid ACT containing amodiaquine in patients taking zidovudine or EFV. - Avoid ACT containing sulfadoxine-pyrimethamine combination if a patient is on CPT. Avoid Intermittent Preventive Treatment (IPT) for malaria in pregnancy if the patient is on CPT.	Refer to a higher-level facility if complicated There is an increased risk of neutropenia with AZT and increased risk of hepatotoxicity with EFV.

Toxoplasmosis	*Toxoplasma gondii*	Fever, reduced alertness, headache, focal neurological deficits, seizures, chorio-retinitis	CSF sample: Dye test, indirect fluorescent antibody test (IFA), enzyme immunoassays (ELISA, immunoblots), agglutination test, avidity test	• Pyrimethamine 100mg stat and 50mg daily with folinic acid 10-25mg daily plus clindamycin 300mg given qds for 6 weeks followed by life-long suppressive therapy until full immunological recovery. or • Cotrimoxazole (Trimethoprim 10mg/kg/day + Sulphamethoxazole 50mg/kg/day) for 4 weeks. Longer therapy may be necessary.	
Scabies	-*Sarcoptes scabei*	Intense itchy lesions most prominent in inter-digital web, spaces of the fingers, wrist, buttocks and axillary area;	Clinical, • Laboratory: Microscopy on KOH prep. of skin scrapings	25% Benzyl benzoate applied whole body, neck down nocte for 3 days OR Permethrin cream 5% applied whole body, neck down and washed	Treat super-imposed bacterial infection with oral antibiotics Treat all household members even if asymptomatic Ivermectin is not recommended for children

		Papular rashes or generalised (Norwegian) Presentation could be more generalized in the context of HIV		off after 8–14 hours. Repeat after 1–2 weeks. If poor response to topical treatment, then oral Ivermectin tablet 200mcg/kg stat, repeat after 7-14 days +/- 25% benzyl benzoate or Crotamiton. Wash and sun-dry/iron clothing, beddings and fomites.	below 15kg and pregnant or lactating women