GUIDELINES FOR TB PREVENTIVE THERAPY IN GHANA

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**ABBREVIATIONS**

ART Antiretroviral treatment

BCG Bacille Calmette-Guérin

CI Confidence interval

CLHIV Children Living with HIV

CPT Co-trimoxazole Preventive Therapy

DR-TB Drug-Resistant TB

DOTS Directly Observed Treatment Short Course

DST Drug Sensitivity Testing

ICF Intensified Case Finding

IGRA Interferon-Gamma Release Assay

IPT Isoniazid Preventive Therapy or Treatment

LTBI Latent Tuberculosis Infection

MDR-TB Multidrug-Resistant Tuberculosis

PLHIV People Living with HIV

SOPs Standard Operating Procedures

TPT Tuberculosis Preventive Therapy

TST Tuberculin Skin Test

TB Tuberculosis

**DEFINITIONS**

The definitions listed below apply to the terms as used in these guidelines.

**Adult**: A person over 19 years of age

**Adolescent:** A person aged 10–19 years.

**Child**: A person under 10 years.

**Infant**: A child under 1 year of age.

**Bacteriologically confirmed TB**: TB diagnosed in a biological specimen by smear microscopy, culture or a WHO-approved molecular test such as Xpert MTB/RIF.

**Close contacts of TB (including DRTB) patients**: People living in the same household as the index patient, or spending many hours a day together with the patient in the same indoor space. Due to the difficulty in tracing contacts of TB clients, contact investigation should be integrated into routine programmatic management of TB and DR-TB

**Contact**: Any person who was exposed to a case of TB (see definition below).

**Contact investigation**: A systematic process for identifying previously undiagnosed cases of TB among the contacts of an index case. In some settings, the goal includes testing for LTBI to identify candidates for preventive treatment. Contact investigation consists of identification and prioritization and clinical evaluation.

**High-TB-incidence country**: A country with a WHO-estimated TB incidence rate of ≥ 100/100 000.

**Household contact**: A person who shared the same enclosed living space as the index case for one or more nights or for frequent or extended daytime periods during the 3 months before the start of current treatment.

**Index case (index patient) of TB**: The initially identified case of new or recurrent TB in a person of any age, in a specific household or other comparable setting in which others may have been exposed. An index case is the case on which a contact investigation is centred but is not necessarily the source case.

**Latent tuberculosis infection (LTBI):** A state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest active TB. There is no gold standard test for direct identification of *Mycobacterium tuberculosis* infection in humans. The vast majority of infected people have no signs or symptoms of TB but are at risk for active TB disease.

**Preventive treatment:** Treatment offered to individuals who are considered to be at risk for TB disease in order to reduce that risk. Also referred to as LTBI treatment or preventive therapy.

**Tuberculosis (TB):** The disease state due to *Mycobacterium tuberculosis*. In this document, commonly referred to as “active” TB or TB “disease” in order to distinguish it from LTBI.

**EXECUTIVE SUMMARY**

Tuberculosis (TB) is the most common opportunistic infection with a high mortality rate among HIV-infected individuals. The risk of TB in HIV-infected persons continues to increase as HIV disease progresses and immunity decreases. There are persons who are HIV negative but are at risk of developing TB disease by virtue of having immunosuppression from medications or disease. It has been found that a vast majority of people infected with TB do not have no signs or symptoms of TB but are at high risk of active TB disease when the immune system becomes compromised. This state is known as Latent TB infection (LTBI) and is defined as ‘a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest active TB(1).

TB Preventive Therapy (TPT) is the administration of one or more anti-tuberculous drugs to individuals with latent TB infection to prevent progression to active disease. WHO recommends the use of Isoniazid for 6 months in resource-limited settings for the prevention of TB in at-risk populations living in high TB incidence, prevalence and transmission settings. The use of Isoniazid is one of the ways in which active TB disease is prevented among at-risk populations in high TB incidence settings. Others include Rifampicin and Isoniazid taken daily for 3 months and Rifapentine plus Isoniazid weekly for 3 months. Among PLHIV, preventing TB entails the 3 ‘I’s: Intensified case finding, Isoniazid Preventive Therapy (IPT), Infection Control for TB plus early initiation of ART. The risk of developing TB disease is reduced by about 60-90% in individuals who are given TPT.

The development of the TB Preventive Therapy Guidelines for Ghana is a milestone in the response towards improving management of TB/HIV co-infection and prevention of TB in those who are HIV-negative but are at high risk of developing TB disease.

**CHAPTER 1**

**1.1 INTRODUCTION**

Tuberculosis(TB) is the most frequent cause of AIDS-related deaths worldwide, despite progress in access to ART(2). It caused about 400 000 deaths among people living with HIV in 2016, representing one third of all HIV deaths. Global data in 2016 indicated that people living with HIV were 21 times (2,3) more likely to develop active TB than those without HIV infection(4). There is a fourfold increase in the number of TB cases registered by national TB programmes, due to the dramatic spread of the HIV epidemic throughout sub-Saharan Africa in the past years. Based on the WHO Global End TB Strategy which includes the objective to reduce TB incidence by 90% by 2035, the National HIV/AIDS Control Programme (NACP) and National TB Programme (NTP) have set out the interventions needed to achieve the interim objective of reducing TB transmission among the most vulnerable populations.

 **1.11 BACKGROUND**

Latent tuberculosis infection (LTBI) is defined as a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest active TB (5). As there is no “gold standard” test for Latent TB Infection (LBTI), the global burden is not known with certainty. However, up to one third of the world’s population is estimated to be infected with *M. tuberculosis*(6–8), and the vast majority have no signs or symptoms of TB disease and are not infectious, although they are at risk for active TB disease and for becoming infectious. Several studies have shown that, on average, 5–10% of those infected will develop active TB disease over the course of their lives, usually within the first 5 years after initial infection(9). The risk for active TB disease after infection depends on several factors, the most important being immunological status (5). Prevention of active TB disease by treatment of LTBI is a critical component of the WHO End TB Strategy (10).

The efficacy of currently available treatments for LTBI ranges from 60% to 90% (2). The potential benefit of treatment should, however, be carefully balanced against the risk for drug-related adverse events. Mass or population-wide LTBI testing and treatment are not feasible because the tests are imperfect, there are risks of serious and fatal side-effects, and the cost would be high, for a strategy of unproven public health impact. For infected individuals in population groups with high risk for progression to active disease compared to the general population the benefits outweigh the harm. Management of LTBI involves a comprehensive package of interventions: identifying and testing those individuals who are exposed, delivering effective, safe treatment in such a way that the majority of those starting a treatment regimen will complete it with no or minimal risk of adverse events. The process should be monitored and evaluated to assess the outcomes.

**1.12 RATIONALE**

The prevalence of TB in Ghana is 282 per 100,000 and incidence is 156 per 100,000 (11). This places Ghana in a high TB incidence category (high TB incidence estimated annual TB incidence rate, ≥ 100 per 100 000 population)(5). Given this background, management of LTBI is recommended for children and adults living with HIV(12) and contacts (adult and children) of people with TB and other clinical risk groups living in settings with a low TB incidence (estimated annual TB incidence rate < 100 per 100 000 population)(5,13,14). There are other at-risk persons who also benefit from LTBI treatment. These include patients with solid organ and haematological transplant, anti-tumour necrosis factor (anti-TNF) treatment, those on dialysis and those with silicosis.

Current WHO guidelines on LTBI is based on the probability that the condition will progress to active TB disease in these specific risk groups, the underlying epidemiology and burden of TB, the availability of resources and the likelihood of a broader public health impact. The WHO recommendations and guidelines led to a significant increase in preventive treatment of TB particularly among people living with HIV but the global coverage of this intervention is still very low(4).

 **CHAPTER 2**

**IDENTIFICATION OF POPULATONS FOR TESTING AND TREATMENT OF LATENT TUBERCULOSIS INFECTION (LTBI)**

Not all individuals infected with *M. tuberculosis* develop active TB. It is estimated that the lifetime risk of an individual with LTBI for progression to active TB is 5–10%(9). The risk is particularly high among children under the age of 5 years and among people with compromised immunity(5). As preventive treatment entails risks and costs, preventive treatment of *M. tuberculosis* infection should be selectively targeted to the population groups at highest risk for progression to active TB disease and who would benefit most from treatment of LTBI.

Programmatic management of LTBI should select treatment that offers lasting protection for the at-risk population. A critical component of programmatic management should therefore be a comprehensive individual clinical assessment that considers the balance between the risks and benefits.

**2.1 ADULTS AND ADOLESCENTS LIVING WITH HIV (AALHIV)**

Adults and adolescents living with HIV, who are unlikely to have active TB should receive preventive treatment of TB as part of a comprehensive package of HIV care. Treatment should be given to these individuals irrespective of the degree of immunosuppression; also to those on antiretroviral treatment (ART), those previously treated for susceptible TB and pregnant women.

**2.2 INFANTS AND CHILDREN LIVING WITH HIV (CLHIV)**

With special consideration of on-going transmission of TB, the following apply:

* All Infants and children living with HIV who are in contact with a case of TB and are investigated for TB should receive 6 months of isoniazid preventive treatment (IPT) if the investigation shows no evidence of TB disease.
* All infants and children living with HIV in whom TB disease has been ruled out and who have no contact with a case of TB should be offered 6 months of IPT as part of a comprehensive package of HIV prevention and care
* All infants and children living with HIV who have been successfully treated for TB and are living in settings with high TB incidence, prevalence and transmission may receive a course of preventive treatment if there is a high risk of re-infection or recurrence. Preventive treatment can be started immediately after the last dose of TB therapy or later, according to clinical judgement.

**2.3 HIV-NEGATIVE HOUSEHOLD CONTACTS OF A PERSON WITH PULMONARY TB**

With special consideration of on-going transmission of TB, the following apply:

* HIV-negative children aged less than 5 years who are household contacts of people with pulmonary TB and who are found not to have active TB after clinical evaluation should be given TB preventive treatment
* Children aged 5 years or more, adolescents and adults who are household contacts of people with pulmonary TB who are found not to have active TB after clinical evaluation may be given TB preventive treatment.

**2.4 OTHER HIV-NEGATIVE AT-RISK GROUPS**

Patients who fit the following criteria should be screened and treated for LTBI:

* Anti-Tumour Necrosis Factor treatment,
* Patient receiving dialysis,
* Patients preparing for or who have had solid organ or haematological transplant and
* Patients with silicosis

It is recognized that people with diabetes, people with harmful use of alcohol, tobacco smokers and underweight people are also at risk of developing TB. However, the benefits of systematic, routine testing and LTBI treatment of these at-risk people do not outweigh the risks, unless they are part of the groups covered in the recommendations.

**2.5 PEOPLE WHO SHOULD NOT BE GIVEN IPT**

* Patients with symptoms of TB should be fully evaluated to rule out TB disease before they can be eligible for IPT
* People with active TB disease
* PLHIV previously treated for MDR TB
* Known or suspected hypersensitivity to Isoniazid
* Chronic liver disease or hepatitis
* Regular or heavy alcohol consumption
* Moderately severe peripheral neuropathy.
* History of convulsions and psychosis
	+ Concomitant medication- phenytoin, carbamazepine, selective serotonin re-uptake inhibitors, antidepressants, oral ketoconazole, itraconazole, warfarin, theophylline, disulfiram

**Testing for Latent TB Infection in PLHIV (adults and paediatrics)**

Note: Testing for latent TB (using Tuberculin Skin Test (TST) or Interferon Gamma Release Assays (IGRAs)) is not required before offering TPT.

All PLHIV (paediatric and adults) should be offered TPT immediately active TB has been ruled out.

**JOB AIDS ON IDENTIFICATION OF AT-RISK POPULATIONS FOR LTBI TESTING AND TREATMENT**

**ELIGIBILITY FOR TPT**

1. All PLHIV who screen negative for TB
2. All HIV negative children under 5 years who have contact with a smear positive TB case and screen negative for TB.
3. Patients receiving dialysis, anti-TNF treatment, solid organ and haematological transplant patients (both pre and post- transplant) and those with silicosis
4. Persons living with HIV who have successfully completed their TB treatment

**CONTRAINDICATIONS FOR TPT**

* Patients with symptoms of TB need to be screened to rule out TB with TB screening tool
* Patients with active TB
* PLHIV previously treated for MDR-TB
* Known or suspected hypersensitivity to isoniazid
* Alcohol use (regular and harmful)
* Chronic liver disease or symptoms of hepatitis (self-reported, right upper quadrant pain, dark urine, yellowing of the eyes (jaundice), pale stools)
* History of convulsions (exclude febrile convulsion in children)
* History of psychosis
* Moderately severe peripheral neuropathy (burning sensation in the limbs)
* Concomitant use of phenytoin, carbamazepine, warfarin, theophylline, disulfiram, SSRIs, antidepressants (citalopram, fluoxetine paroxetine, sertraline), oral ketoconazole or itraconazole

**CHAPTER 3**

**ALGORITHMS FOR RULING OUT ACTIVE TB DISEASE**

**Introduction**

It is necessary to rule out active TB in a patient before starting TPT. The following algorithms are to be followed to facilitate the exclusion of active TB. Where asterix (\*) are indicated it implies further investigations are required by a health care worker with a higher expertise to ensure TB is ruled out and other conditions are not missed. It is recognized that some facilities may not have the digital Chest-X-Ray facilities provided by the NTP. The absence of this should not be a barrier for implementing these algorithms.

**Group A algorithms**

These are to be followed for screening children who have a history of contact with a suspected or confirmed TB patient, whether HIV infected or not.

Part A algorithm is for children with signs and symptoms.

Part B algorithm for children with no signs and symptoms.

**Part A - Algorithm for Screening and Diagnosis of TB in <5 Children who are household contacts of people with TB**

**Children who are household contacts of people with PTB**

**NO sign & symptom: Go to Part B**

**Any signs and symptoms for TB (poor weight gain, fever, current cough, history of contact with TB Patient)**

**GeneXpert MTB/RIF test/Gastric lavage/Sputum for AFB and other applicable samples.**

**MTB not detected**

**MTB detected**

**Chest X-ray (CXR) if available**

**Rifampicin Resistant**

**Rifampicin Sensitive**

**Initiate MDR-TB Therapy, Conduct LPA/ Culture & DST**

**CXR Abnormal**

**CXR Normal**

**Initiate Anti-TB Therapy**

**\*\*Further Evaluation**

TPT

**Note:\*\*\*Further evaluation should involve an expert opinion**

**Most children MTB will not be detected. MDR-TB is determined using adult contact results as surrogate.**

**Part B - Algorithms for Screening and Diagnosis of TB in <5 Children who are household contacts of people with TB**

**No TB signs and symptoms**

**Chest X-Ray Not Available**

**Chest X-Ray Available**

**CXR Abnormal**

**CXR Normal**

**TB Preventive Therapy (TPT)**

**GeneXpert MTB/Rif test**

**MTB detected**

**\*\*\*MTB not detected: evaluate further**

**Rifampicin Sensitive**

**Rifampicin Resistant**

**Initiate anti-TB Therapy**

**Initiate MDR-TB Therapy, Conduct LPA/ Culture & DST**

 **Note:\*\*\* MTB not detected; further evaluation should involve an expert opinion**

**Group B algorithms**

These are to be followed for all confirmed HIV- infected patients (children, adolescents and adults).

**Part A - Algorithm for Screening and Diagnosis of TB in Adult and Adolescent living with HIV**

 **Interview for signs and Symptoms**

**NO sign & symptom:**

**Go to Part B**

**Any signs and symptoms for TB (cough of any duration, night sweats, chest pain, weight loss, fever) present**

**GeneXpert MTB/RIF test**

**MTB not detected**

**MTB detected**

**Rifampicin Resistant**

**Rifampicin Sensitive**

**Chest X-ray (CXR) if available**

**Initiate MDR-TB Therapy, Conduct LPA/ Culture & DST**

**CXR Abnormal**

**CXR Normal**

**Initiate Anti-TB Therapy**

**\*\*\*Further Evaluation**

**TPT**

 **Note:\*\*\*Further evaluation should involve an expert opinion**

**Part B - Algorithms for Screening and Diagnosis of TB in Adults and Adolescent Living with HIV**

**No TB signs and symptoms**

**Chest X-Ray Not Available**

**Chest X-Ray Available**

**CXR Normal**

**CXR Abnormal**

**GeneXpert MTB/Rif test**

**TB Preventive Therapy (TPT)**

**\*\*\*MTB not detected: evaluate further**

**MTB detected**

**Rifampicin Sensitive**

**Rifampicin Resistant**

**Initiate MDR-TB Therapy, Conduct LPA/ Culture & DST**

**Initiate anti-TB Therapy**

**Note:\*\*\* MTB not detected ; Further evaluation should involve an expert opinion**

**Algorithm for Screening and Diagnosis of TB in Children living with HIV- Part A**

**Children living with HIV**

**NO sign & symptom: Go to Part B**

**Any signs and symptoms for TB (poor weight gain, fever, current cough, history of contact with TB Patient)**

**GeneXpert MTB/RIF test/Gastric lavage/Sputum for AFB and other applicable samples.**

**MTB detected**

**MTB not detected**

**Rifampicin Resistant**

**Rifampicin Sensitive**

**Chest X-ray (CXR) if available**

**Initiate MDR-TB Therapy, Conduct LPA/culture & DST**

**Initiate Anti-TB Therapy**

**CXR Abnormal**

**CXR Normal**

**TPT**

**\*\*Further Evaluation**

**Note:\*\*\*Further evaluation should involve an expert opinion**

**Algorithms for Screening and Diagnosis of TB in Children living with HIV – Part B**

**No TB signs and symptoms**

**Chest X-Ray Available**

**Chest X-Ray Not Available**

**CXR Abnormal**

**CXR Normal**

**TB Preventive Therapy (TPT)**

**GeneXpert MTB/Rif test**

**MTB not detected: evaluate further**

**MTB detected**

**Rifampicin Sensitive**

**Rifampicin Resistant**

**Initiate anti-TB Therapy**

**Initiate MDR-TB Therapy, Conduct LPA/ Culture & DST**

**Note:\*\*\* MTB not detected; further evaluation should involve an expert opinion**

**Algorithm for Screening and Diagnosis of TB in HIV negative children > 5years and who are household contacts of people with TB and other at risk Populations Part-A**

**Ask for any symptoms of TB from individuals from the risk group**

**Any signs and symptoms for TB (ie poor weight gain, fever, current cough, history of contact with TB Patient) present**

**NO sign & symptom:**

**Go to Part B**

**GeneXpert MTB/RIF test/Gastric lavage/Sputum for AFB and other applicable samples.**

**MTB detected**

**MTB not detected**

**Chest X-ray (CXR) if available**

**Rifampicin Resistant**

**Rifampicin Sensitive**

**CXR Normal**

**CXR Abnormal**

**Initiate MDR-TB Therapy, Conduct LPA/ Culture & DST**

**Initiate Anti-TB Therapy**

**\*\*Further Evaluation**

**InitiateTPT**

**Note:\*\*\* MTB not detected; further evaluation should involve an expert opinion**

**Algorithms for Screening and Diagnosis of TB in HIV negative children > 5years and who are household contacts of people with TB and other at risk Populations- Part B**

 **No TB signs and symptoms**

**TST or IGRA**

**Positive**

**Negative**

**Chest X-ray**

**Normal X-ray**

**Abnormal x-ray**

**TPT**

**Evaluate further**

**SOPs for Screening and Diagnosing of TB in Adults and Adolescents living with HIV**

* Client visits the facility (ART Center, TB Center, and or ART /TB Collaborative centre)
* Screen client using TB symptom screening tool
* For those who respond” yes” to any of the signs and symptoms (i.e. cough of any duration, night sweat, chest pains, weight loss and fever) should be referred for a GeneXpert test.
* If MTB is detected;
	+ Initiate anti TB therapy if Rifampicin is sensitive.
	+ If client is Rifampicin resistant refer to regional MDR TB
* For clients who test negative for MTB :
* Do a chest x-ray if available in the facility.
	+ If chest X-ray is abnormal refer client for further evaluation.
	+ If chest X-ray is normal, initiate client on TPT.

For those who have no signs and symptoms after applying the symptoms screening tool.

* Do a chest x-ray if available
	+ If chest X-ray is normal, initiate client on TPT.
	+ If chest x-ray is abnormal refer client for a GeneXpert test
* If MTB is detected;
	+ Initiate anti TB therapy if Rifampicin is sensitive.
	+ If client is Rifampicin resistant refer to regional MDR TB
* For clients who test negative for MTB refer client to TB expert for further evaluation
	+ If chest x-ray is not available
	+ Initiate TPT

**SOPs for Screening and Diagnosing TB in children living with HIV**

* Child visits the facility (Paediatric clinic, ART Center, TB Center, and or ART /TB Collaborative centre)
* Screen child using TB symptom screening tool including history of contact with TB patient or patient with chronic cough.
* For a ”yes” response to any of the signs and symptoms (ie cough of any duration, night sweat, chest pains, weight loss, fever, history of contact with TB patient or patient with chronic cough) child do chest Xray or consider referral for a GeneXpert
* If MTB is detected;
	+ Initiate anti TB therapy if Rifampicin is sensitive.
	+ If Rifampicin resistant refer to regional MDR TB
* For a child who tests negative for MTB :
* Do a chest x-ray if available in the facility.
	+ If chest X-ray is abnormal refer the child to TB expert for further evaluation.
	+ If chest X-ray is normal, initiate the child on PTP.
* If chest X-ray is not available refer for further evaluation\*\*\*
	+ \*\*\* Further evaluation-to be done by persons with higher expertise, physicians, paediatricians, MO

For those who have no signs and symptoms after applying the symptoms screening tool.

* Do a chest x-ray if available
	+ If chest X-ray is normal, initiate the child on TPT.
	+ If chest x-ray is abnormal refer the child for a GeneXpert test
* If MTB is detected;
	+ Initiate anti TB therapy if Rifampicin is sensitive.
	+ If Rifampicin resistant refer to regional MDR TB
* For a child who tests negative for MTB refer the child to TB expert for further evaluation
	+ If chest x-ray is not available
	+ Initiate the child on TPT

**SOPs for Screening and Diagnosing TB in HIV-negative Children < 5 years who are household contacts of people with PTB.**

* Screen child using TB symptom screening
* If a “yes” response to any of the symptoms (ie cough of any duration, night sweat, chest pains, weight loss, fever, history of contact with TB patient or patient with chronic cough) should be referred for a chest Xray and or GeneXpert test.
* If MTB is detected;
* Initiate anti TB therapy if Rifampicin is sensitive.
	+ If child is Rifampicin resistant refer to regional MDR TB
* For a child who tests negative for MTB:
* Do a chest x-ray if available in the facility.
	+ If chest X-ray is abnormal refer the child to TB expert for further evaluation.
	+ If chest X-ray is normal, initiate the child on TPT.

For those who have no signs and symptoms after applying the symptoms screening tool.

* Do a chest x-ray if available
* If chest X-ray is normal, initiate the child on TPT.
* If chest x-ray is abnormal refer the child for a GeneXpert test
* If MTB is detected;
* Initiate anti TB therapy if Rifampicin is sensitive.
* If the child is Rifampicin resistant conduct a culture and DST and per the results initiate MDR
* For a child who tests negative for MTB refer the child to TB expert for further evaluation
* If chest x-ray is not available
* Initiate the child on TPT

**SOPs for Screening and Diagnosing TB in HIV negative children ≥ 5years and who are household contacts of people with TB and other at risk populations\*\***

* Screen individuals from the risk group for symptoms of TB (ie cough of any duration, haemoptysis, night sweats, chest pains, weight loss, fever and shortness of breath)
* If “yes” to any of the symptoms above, refer for further evaluation
* If no to any of the symptoms above, do TST or IGRA
* If positive to IGRA or TST do a chest x-ray
* If chest x-ray is abnormal refer for further evaluation
	+ \*\*\* Further evaluation-to be done by TB/HIV or persons with higher expertise, physicians, paediatricians, MO
* If chest x-ray is normal initiate TPT

\*\* Refer Chapter 2

**CHAPTER 4**

**TREATMENT OPTIONS FOR LATENT TUBERCULOSIS INFECTION**

**First option**

Isoniazid monotherapy for 6 months is recommended for treatment of LTBI in both adults and children

**Second option**

Rifapentine and isoniazid weekly for 3 months may be offered as an alternative to 6 months of isoniazid monotherapy as preventive treatment for both adults and children.

Recommended dosages of drugs for the treatment of LTBI

|  |  |  |
| --- | --- | --- |
| Drug regimen | Dose  | Maximum dose |
| Isoniazid alone, daily for 6 months | Adults, 5 mg/kg Children, 10 mg/kg | 300 mg |
| Weekly rifapentine\* plus isoniazid for 3 months (12 doses) | Individuals aged ≥12 years: Isoniazid: 15 mg/kg Individuals aged 2–11 years: isoniazid: 25 mg/kg Rifapentine:10.0–14.0 kg = 300 mg14.1–25.0 kg = 450 mg25.1–32.0 kg = 600 mg32.1–50.0 kg = 750 mg> 50 kg = 900 mg | Isoniazid, 900 mgRifapentine, 900 mg |

 **\* Regimens containing rifapentine should be prescribed with caution to PLHIV who are on PI -based ART & Nevirapine-based ART because of potential drug–drug interactions**.

**Special Circumstances**

|  |  |
| --- | --- |
| Patients previously treated for TB *(Secondary prophylaxis*)  | All PLHIV who have successfully completed treatment for TB disease should receive TPT for an additional six months. TPT can be started immediately after the last dose of anti-TB therapy or at a later date.  |
| Patient on TPT develops TB during TPT treatment  | If patient develop TB symptoms during IPT treatment do the following: 1. Evaluate patients for TB. Do DST for isoniazid, rifampicin, aminoglycosides and fluoroquinolones where available. Treat according to resistance pattern. 2. If no resistance, treat for normal TB. |
| IPT in children born to smear positive mothers: | If a baby is born to a mother with TB (irrespective of type of TB), assess the newborn for TB. Non-specific features suggestive of neonatal TB include: Fever, low birth weight, hepato- splenomegaly, irritability, feeding intolerance. If the child has none of the above, give IPT for 6 months. Withhold BCG until 2weeks after completion of IPT. |
| IPT and MDR-TB | Contacts of MDR TB and PLHIV with DR TB are not eligible for IPT. |

**JOB AIDES FOR TREATMENT OPTIONS**

**OPTION 1**

Isoniazid monotherapy for 6 months is recommended for treatment of LTBI in both adults and children in Ghana.

**Dose of INH for TPT**

**CHILDREN**

|  |  |  |  |
| --- | --- | --- | --- |
| **Weight Range(kg)** | **Dose in mg** | **Number of 100mg tablet** | **Number of 300mg tablet** |
| < 5 | 50 | ½ tablet | Not recommended |
| 5.0 -9.9 | 100 | 1 tablet | Not recommended |
| 10.0-13.9 | 150 | 1 ½ tablet or  | ½ |
| 14.0-19.9 | 200 | 2 tablets | Not recommended |
| 20.0-24.9 | 250 | 2 ½ tablets | Not recommended |
| ≥25 | 300 | 3 tablets or  | 1 tablet |

**Dose of INH for TPT**

**ADULTS**

|  |  |  |  |
| --- | --- | --- | --- |
| **Weight Range(kg)** | **Dose in mg** | **Number of 100mg tablet** | **Number of 300mg tablet** |
| 20-30 | 150 | 1 ½ tablet | ½ tablet |
| 31-40 | 200 | 2 tablets | - |
| >40 | 300 | 3 tablets | 1 tablet |

**OPTION 2**

Rifapentine and Isoniazid weekly for 3 months may be offered as an alternative to 6 months of isoniazid monotherapy as preventive treatment for both adults and children in Ghana.

**Dose of Rifapentine plus Isoniazid**

|  |  |  |
| --- | --- | --- |
| **Drug Regimen** | **Dose**  | **Maximum Dose** |
| Weekly Rifapentine plus isoniazid for 3 months(12doses) | Individuals aged ≥12 years: Isoniazid:15mg/kgIndividuals aged 2-11 years: Isoniazid:25mg/kgRifapentine:10.0-14.0 kg = 300mg14.1-25.0 kg = 450mg25.1-32.0 kg = 600mg32.1-50.0 kg = 750mg>50kg = 900mg | Isoniazid, 900mgRifapentine, 900mg |

**NB: This option is for PLHIV and should be administered at a secondary and tertiary facility because of drug interactions.**

**All clients who are on TPT should also receive Pyridoxine.**

**Dosages for Pyridoxine**

|  |  |  |  |
| --- | --- | --- | --- |
| **Weight Range(kg)** | **Dose in mg** | **Number of 50mg tablet** | **Number of 100mg tablet** |
| <25 | 25 | ½ tablet | ¼ tablet |
| ≥25 | 50 | 1 tablets | ½ tablet |

In special circumstances, kindly follow the table below;

|  |  |
| --- | --- |
| **SCENARIO** | **ACTION(S)** |
| **Patients previously treated for TB** ***(Secondary prophylaxis*)**  | All PLHIV who have just successfully completed treatment for TB disease should receive INH for an additional six months. * All PLHIV who have been successfully treated for TB and are living in settings with a high TB prevalence and transmission should receive TPT for an additional six months at the same doses above. TPT can be started immediately after the last dose of anti-TB therapy or at a later date.
 |

|  |  |
| --- | --- |
| **SCENARIO** | **ACTION(s)** |
| **Patient on TPT develops TB during TPT treatment**  | * Stop TPT
* Treat patient for TB
* Administer TPT for 6 months after the TB treatment

  |
| **TPT in children 0-5 years with contact with smear positive patients** | * Administer TPT for 6 months after ruling out active TB disease
 |

**CHAPTER 5**

**GUIDE FOR MONITORING CONTACTS OF TB CLIENTS**

‘Close contacts’ of TB (including DRTB) patients are defined as people living in the same household as the index patient, or spending many hours a day together with the patient in the same indoor space. Due to the difficulty in tracing contacts of TB clients, contact investigation should be integrated into routine programmatic management of TB and DR-TB.

**GROUPS TO BE INVOLVED IN CONTACT MONITORING**

**Patient**. Contact investigation starts with the education of the TB patient. Patients

should be educated about the infectiousness of their disease and the high risk of transmission

to contacts who share the same living space. While they should not be unduly alarmed, they

should be informed that their family members are likely already infected with TB,

so the most important intervention is to monitor them closely for symptoms of active TB.

**Family.** One of the most important reasons to do a home visit for every TB patient at

the initiation of TB treatment is to do contact investigation. A community nurse or

health care provider should educate the family that they are all likely already infected with

TB, and explain the importance of notifying the community or clinical team quickly

about family members who develop symptoms of active TB.

**Clinical team.** The clinical team has multiple opportunities to inquire about the health

of the TB patient’s family contacts. At every clinical evaluation, doctors and nurses

should ask the patient whether any family member has developed TB symptoms.

 **Community nurses or health care providers educated on TB**. During home visits

to check adherence or assess the social situation, the community nurse should inquire if

there are any family members who have developed symptoms of active TB. The community

nurse may also directly interview the family members at their home. Community nurses are

also best suited to address fears or doubts about the health system or other social barriers to

treatment for TB contacts.

**Community volunteers:** community volunteers, who are the closest to the

family and are most likely to identify family members with TB symptoms can be involved in contact tracing. This is particularly true for members of the extended family who visit periodically.

**DIAGNOSTIC WORK UP FOR ADULTS WITH TB SYMPTOMS**

1. An evaluation by a healthcare provider, including history and physical examination;
2. A chest xray
3. Sputum investigations (ideally a rapid diagnostic method such as Xpert MTB/RIF, or if not available, sputum smear microscopy; culture and drug susceptibility testing (DST))
4. HIV testing.
* If the initial investigation is not suggestive of active TB, the household contact should continue to be monitored closely by the clinical team.

**DIAGNOSTIC WORK UP FOR PAEDIATRIC CONTACTS WITH TB SYMPTOMS**

1. An evaluation by a healthcare provider, including history and physical examination
2. A chest xray
3. Tuberculin skin testing with purified protein derivative (older child due to effect of BCG )
4. Sputum investigations (ideally a rapid diagnostic method such as Xpert MTB/RIF, or if not available, sputum smear microscopy; culture and DST)
5. HIV testing

\*Follow algorithm for household contacts found to be negative for active TB.

\*There is no need for TPT in close contacts of MDRTB clients

**CHAPTER 6**

**Monitoring of adverse events**

**Definitions:**

**Adverse Event**

An adverse event is a medical occurrence temporally associated with the use of a medicinal product, but not necessarily causally related.

**Adverse reactions**

A response to a drug which is noxious and unintended, and which occurs at doses normally used in individuals for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function.

 Adverse reactions have been associated with isoniazid use (asymptomatic elevation of serum liver enzyme concentrations, peripheral neuropathy and hepatotoxicity)

 Rifapentine (cutaneous reactions, hypersensitivity reactions, gastrointestinal intolerance and hepatotoxicity).

**Reviews**

HIV negative clients receiving TPT should be monitored routinely at monthly visits. PLHIV receiving TPT should be monitored at their regular ART review visits.

Health care providers should explain the rationale of the treatment, importance of completing it and the possible side effects and actions to be taken.

Patients receiving TPT should be advised to contact their health care provider at any

time if they become aware of symptoms such as;

* Anorexia (lack of appetite for food)
* Nausea
* Vomiting
* Abdominal discomfort
* Persistent fatigue or weakness
* Paraesthesia and numbness

Advice clients receiving TPT to stop the treatment and immediately report to the health facility if they experience any of the following symptoms:

* Dark-coloured urine
* Pale stools
* Yellowing of the eyes (Jaundice)
* Significant abdominal pain
* Convulsions

Health care providers should advise clients put on TPT to volunteer information on medication history if they experience any of the above listed symptoms but present to a health facility other than the facility where TPT was initiated.

Evaluate patient, do a liver function test and manage appropriately.

**NB: Health providers should remember to complete the Adverse Drug Reaction form.**

**JOB AIDE ON MONITORING ADVERSE EVENTS**

Adverse reactions have been associated with isoniazid (asymptomatic elevation of serum liver enzyme concentrations, peripheral neuropathy and hepatotoxicity) and rifapentine (cutaneous reactions, hypersensitivity reactions, gastrointestinal intolerance and hepatotoxicity) use.

**Reviews**

* HIV negative clients receiving TPT should be monitored routinely at monthly visits.
* PLHIV receiving TPT should be monitored at their regular ART review visits.
* Explain to the client the rationale of TPT, importance of completing it, possible side effects and actions to be taken.
* Advise patients receiving TPT to report to the health facility at any time if they become aware of symptoms such as;
* Anorexia (lack of appetite for food)
* Nausea
* Vomiting
* Abdominal discomfort
* Persistent fatigue or weakness
* Numbness of the limbs
* Advise clients on TPT to stop treatment and report immediately to the health facility if they experience the following symptoms:
* Dark-coloured urine
* Pale stools
* Jaundice
* Advise clients on TPT to volunteer information on their medication history if they experience any of the above listed symptoms but present to a health facility other than the facility where TPT was initiated.
* Evaluate patient who reports with any of the above symptoms, do a liver function test and manage appropriately.
* **NB: Complete the Adverse Drug Reaction forms and give to appropriate person responsible as early as possible**

**CHAPTER 7**

**Adherence to and completion of preventive treatment**

It is important to educate patients on the TB disease process, rationale and benefits of TPT. Strict adherence to and compliance with TPT is essential for the patient to achieve the benefit of TPT. Adherence should be assessed and reinforced at every visit. Screen clients for active TB using the algorithm for screening and diagnosis of TB at every visit.

**Job Aide**

**Adherence to and completion of preventive treatment**

* Explain the reason and benefit of TPT to the client
* Educate client of the dosage and duration of TPT
* Educate client on side effects and what to do
* Assess adherence by patient self-report and/or pill count at every visit
	+ If there is evidence of non-adherence, explore the reason and counsel accordingly
		- If patient discontinue for <1mth, assess, counsel and continue
		- If patient discontinue for >1mth, assess, counsel and investigate for active TB then restart TPT if patient show commitment
		- If patient discontinue for more than 3mths or more than once, do not reinitiate
* Screen for active TB among all clients at every visit using the Tb screening tool
	+ If TB is found, Stop TPT and treat
* At the end of the 6mth inform client that TPT has been completed and congratulate client
	+ Educate the client report to the clinic with any signs and symptoms of TB

**CHAPTER 8**

**MONITORING AND EVALUATION**

Surveillance of TPT implementation will be done using the indicators below. The district health coordinators (for TB, HIV or TB/HIV collaborative programmes) will submit data on monthly and quarterly basis to district and national management teams. The reports will contain but are not limited to the national indicators set.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Indicator** | **Numerator** | **Denominator** | **Purpose** | **Source** |
| Number of PLHIV newly enrolled in HIV care  | N/A | N/A | To help with projections and forecasting of commodity needs | Monthly summary form for ART |
| Number of PLHIV screened for TB | N/A | N/A | To help with projections and forecasting of commodity needs | Monthly summary screening tool |
| Number of PLHIV newly enrolled in HIV care screened for TB  | N/A | N/A | To help with projections and forecasting of commodity needs | Monthly summary screening tool |
| Number of PLHIV newly enrolled who are eligible for TPT | N/A | N/A | To help with projections and forecasting of commodity needs | Monthly summary screening tool |
| Number of PLHIV newly enrolled in HIV care started on TPT | N/A | N/A | To help with projections and forecasting of commodity needs | Monthly summary form for ART |
| Total number of PLHIV newly enrolled who received and completed TPT |  |  |  |  |
| Proportion of PLHIV newly enrolled in HIV care screened for TB | Number of PLHIV newly enrolled in HIV care screened for TB | Number of PLHIV newly enrolled in HIV care  | Measure the capacity of the programme to detect active TB among PLHIV | DHIMS |
| Proportion of PLHIV newly enrolled who are eligible and received TPT | Number of PLHIV newly enrolled who are eligible and received TPT | Number of PLHIV newly enrolled who are eligible for TPT | Measure the capacity of the programme to initiate TPT among PLHIV | DHIMS |
| Treatment completion rate | Total number of PLHIV newly enrolled who received and completed TPT | Total number of PLHIV newly enrolled who were imitated on TPT 9 months ago |  |  |
| Total number of children under 5 who are household contacts of PTB cases screened  | NA | NA | To help with projections and forecasting of commodity needs | Monthly summary screening tool |
| Total number of children under 5 who are household contacts of PTB cases | NA | NA | To help with projections and forecasting of commodity needs |  |
| Total number of children under 5 who were eligible and received TPT | N/A | N/A | To help with projections and forecasting of commodity needs |  |
| Total number of children under 5 who were eligible for TPT | N/A | N/A | To help with projections and forecasting of commodity needs |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Indicator** | **Numerator** | **Denominator** | **Purpose** | **Source** |
| Total number of children under 5 who are household contacts of PTB cases who were screened | Total number of children under 5 who are household contacts of PTB cases who were screened | Total number of children under 5 who are household contacts of PTB cases | Measure the capacity of the programme to detect active TB among children <5 who are household contacts of PTB cases | DHIMS |
| Proportion of children under 5 who are household contacts of PTB cases who were eligible and received TPT | Total number of children under 5 who were eligible and received TPT | Total number of children under 5 who were eligible for TPT | Measure the capacity of the programme to initiate TPT among children <5 who are household contacts of PTB cases | DHIMS |
| Total number of children under 5 who received and completed TPT | N/A | N/A |  |  |
| Treatment completion rate | Total number of children under 5 who received and completed TPT | Total number of children under 5 who were imitated on TPT 9 months ago |  |  |
| Total number of eligible individuals in at risk populations tested for LTBI | N/A | N/A | To help with projections and forecasting of commodity needs |  |
| Total number of eligible individuals in at risk populations tested for LTBI and received TPT | N/A | N/A | To help with projections and forecasting of commodity needs | Decision later |
| Proportion of eligible individuals in at risk populations tested for LTBI and received TPT | Total number of eligible individuals in at risk populations tested for LTBI and received TPT | Total number of eligible individuals in at risk populations tested for LTBI | Measure the capacity of the programme to detect active TB among eligible individuals in at risk populations |  |
| Proportion of eligible individuals in at risk populations tested for LTBI and received TPT and completed the TPT | Total number of eligible individuals in at risk populations tested for LTBI and received TPT and  |  |  |  |

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