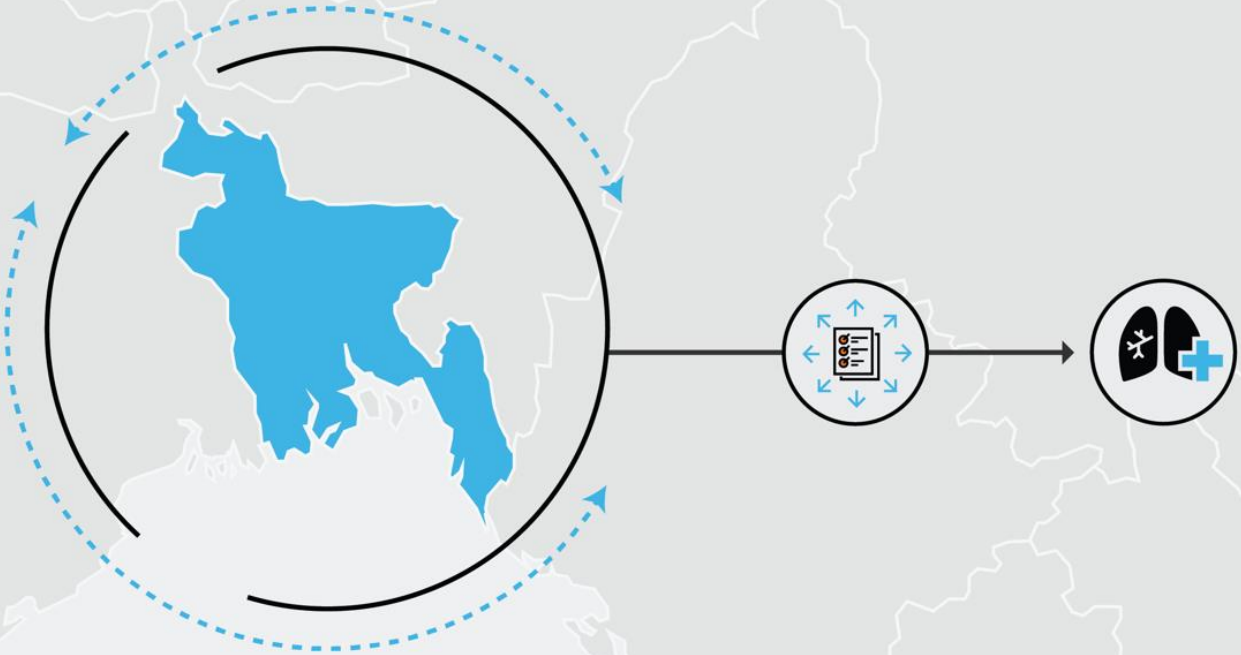
Tuberculosis Preventive Treatment Standard Operating Procedure

National Tuberculosis Control Programme
Bangladesh

APRIL 2021



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ABBREVIATIONS

1HP	1 month of Isoniazid and Rifapentine daily
3HP	3 months of Isoniazid and Rifapentine weekly
3HR	3 months of Isoniazid and Rifampicin daily
4R	4 months of Rifampicin daily
6H	Six months of Isoniazid daily
ACF	Active case finding
AE	Adverse Event
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ART	Antiretroviral Therapy
ARV	Antiretroviral
BC	Bacteriologically confirmed
BPNS	Brief peripheral neuropathy scoring system
CHW	Community health worker
CI	Contact Investigation
CKD	Chronic kidney disease
CxR	Chest X-ray
DR-TB	Drug-resistant tuberculosis
DS-TB	Drug susceptible tuberculosis
Gx	GeneXpert
H/INH	Isoniazid
HA	Health assistant
HIV	Human Immunodeficiency Virus
IGRA	Interferon-Gamma Release Assay
LFT	Liver function test
LTBI	Latent tuberculosis infection
MDR-TB	Multi-drug resistant tuberculosis
NGO	Non-governmental organization
NTP	National Tuberculosis Program
PLHIV	People living with HIV

R/Rif	Rifampicin
SOP	Standard Operating Procedure
TB	Tuberculosis
TLCA	Tuberculosis and leprosy control assistant
TNF	Tumor necrosis factor
TPT	Tuberculosis preventive treatment
UHFPO	Upazilla Health Family Planning Officer
ULN	Upper limit of normal
UN	United Nations
USAID	United States Agency for International Development
WHO	World Health Organization

Disclaimer

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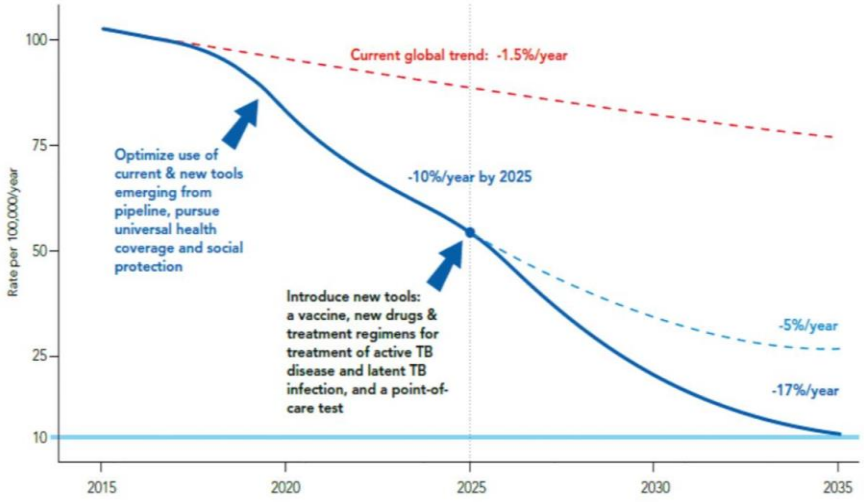
CONTENTS

INTRODUCTION

Although the World Health Organization (WHO) estimates that approximately 23% of the world's population has latent tuberculosis infection (LTBI), the prevalence is significantly higher in the WHO South East Asia region where Bangladesh is located. A modelling study from 2014 estimated that there are approximately 44 million people with LTBI in Bangladesh, or 26.7% of the total population, of whom 10% are below 15 years of age.[1] With a deceleration in the decline in tuberculosis (TB) incidence, it can be assumed that the prevalence of LTBI in Bangladesh has not significantly changed in recent years. To achieve the steep decline in TB incidence necessary to reach TB elimination, optimizing TB case finding and treatment of active disease may not be sufficient, but should be combined with enhanced TB preventive treatment (TPT) coverage along with the use of currently available new tools and those in the pipeline for diagnosis, treatment and prevention, including a vaccine as depicted in Figure 1.

Figure 1: Projected acceleration of the decline in global TB incidence rates



Source: World Health Organization, The End TB Strategy

At the High-level United Nations (UN) Meeting on TB in 2018, the world set global targets to providing TPT to 30 million people by 2022, including 6 million people living with human immunodeficiency virus (PLHIV), 4 million under five children and 20 million other household contacts of people affected by TB. Bangladesh developed a national TPT expansion plan including ambitious TPT targets as in Table 1.

Table 1. Bangladesh targets for TPT coverage from 2021-2025:

Target groups	2021	2022	2023	2024	2025
Adults	118,670	214,099	275,612	367,905	466,521
Children	60,758	70,201	72,728	81,094	82,478
PLHIV *	6,132	1,000	1,000	1,000	1,000
Total	185,560	285,300	349,340	450,000	550,000

*By 2021 all currently identified PLHIV patients will be enrolled on TPT. From 2022 onwards only newly diagnosed patients will be targeted for TPT.

[1] The Global Burden of Latent Tuberculosis Infection: A Re-estimation Using Mathematical Modelling
Rein M. G. J. Houben, Peter J. Dodd, https://doi.org/10.1371/journal.pmed.1002152.s007

To help reach these goals, in 2018 WHO recommended new shorter TPT regimens along with expansion of target groups. TPT should now be provided to all household contacts without active TB disease, regardless of age rather than limiting it to children under 5 years old. In 2020, WHO published a very thorough and comprehensive operational handbook on TPT which included recommendations on one additional newer shorter TPT regimen. The National Tuberculosis Control Program (NTP) of Bangladesh has adopted the new WHO recommendations including the use of shorter TPT regimens and expansion of TPT provision to all household contacts.

OBJECTIVES

- To recognize the importance of LTBI in fueling the TB epidemic
- To become familiar with population groups at high risk for LTBI
- To understand how to rule out active TB disease among those who are potentially eligible for TPT
- To equip providers with the knowledge and skills to provide quality TPT to people with LTBI

INTENDED USERS

This standard operating procedure (SOP) is intended for TB implementers, program managers, programmatic staff, service providers, and community health workers. It will serve as a guide with strategies, procedures and tools that may help address barriers and ensure effective TPT implementation.

DEFINITION OF TERMS

TB preventive treatment (TPT): is treatment offered to individuals at risk of developing active TB disease. Also referred to as treatment of LTBI or TB infection.

TB disease: is when mycobacteria tuberculosis bacilli are actively multiplying in the lungs and/or other organs and the immune system is unable to contain it. TB disease is accompanied by various signs and symptoms including cough, weight loss, fever, night sweats, chest pain, hemoptysis, fatigue, decreased appetite and others depending on the site affected.

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

Latent tuberculosis infection (LTBI): is a state of persistent immune response to stimulation by M. tuberculosis antigens with no evidence of clinically manifest TB disease. There is no gold standard test for direct identification of M. tuberculosis infection in humans. Most infected people have no signs or symptoms of TB but are at risk for TB disease. LTBI is sometimes referred to as just “TB infection”.

Contact investigation: is a systematic process for identifying previously undiagnosed people with TB disease and LTBI among the household contacts of an index TB patient. Contact investigation (CI) consists of identification, clinical evaluation and TPT (for those without TB disease).

Household Contact: is any individual who was living with the index patient in the same house.

Index TB patient: is the first person diagnosed of any age with new or recurrent bacteriologically confirmed TB in the household. An index patient is the person on whom a contact investigation is centered but is not necessarily the source.

Close contact: a person who is not in the household but shared an enclosed space with the index person with TB during the 3 months before the commencement of the current treatment episode.

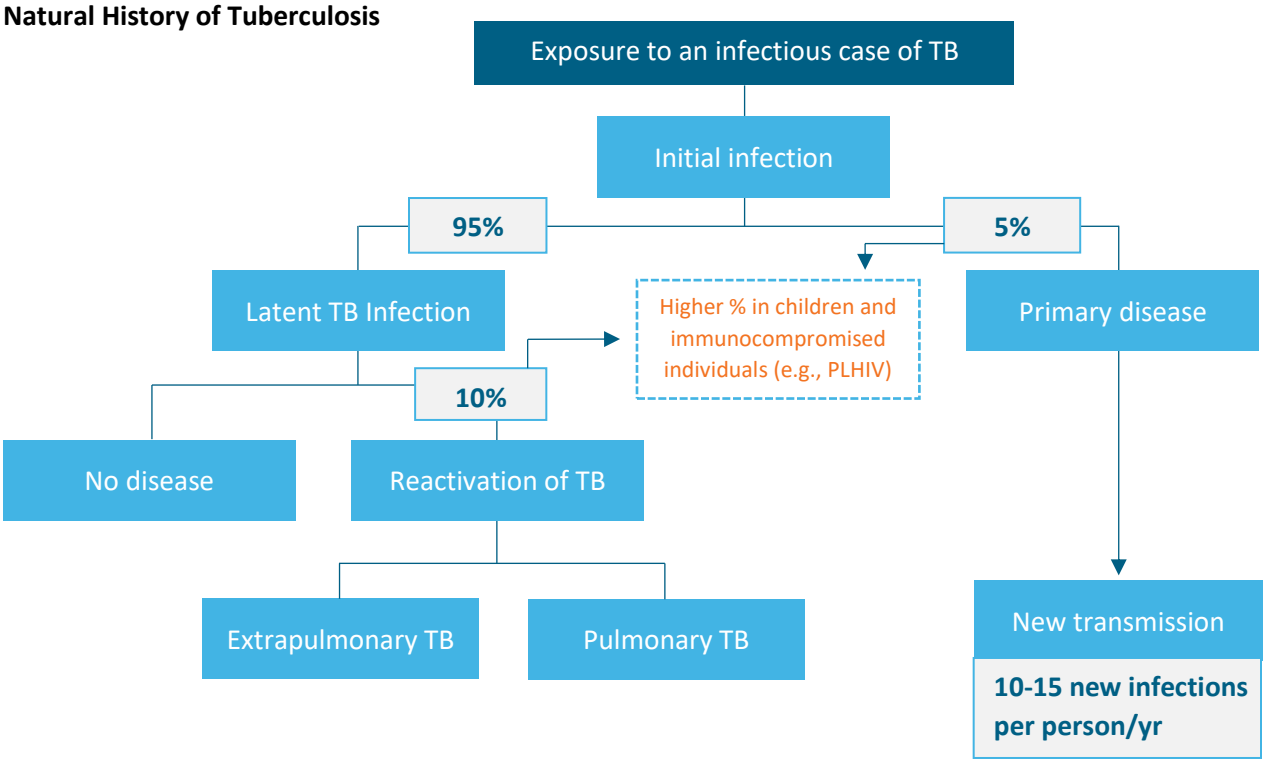
Source case: a person with infectious TB (usually bacteriologically positive pulmonary TB) who transmits the infection to one or more other individuals.

NATURAL HISTORY OF TB

TB primarily spreads from person-to-person through airborne transmission. It is estimated that each infectious individual can infect up to 10-15 people with TB each year until started on treatment and rendered non-infectious. Studies have documented an infection rate of 30 to 50% amongst household contacts of infectious adults with the infection rate in children under 5 as high as 72%.[2, 3] Of those infected with TB, 5% develop primary TB disease, while 95% acquire dormant TB bacilli in the lungs without manifesting any signs of symptoms of TB disease, which is LTBI. Those with LTBI have a 5-10% lifetime risk of the dormant TB bacilli becoming reactive, multiplying and causing TB disease. However, the risk of developing TB disease from TB infection is higher in those with immunocompromise, such as PLHIV who have a 10-15% yearly risk.[4,5] In addition, household contacts under 5 years old have a 15-20% risk of reactivated TB disease.[6] Other risk groups include the elderly over age 60, diabetics, smokers, those with silicosis, substance abuse history, chronic kidney disease (CKD) and specific immunocompromised groups, such as persons on renal dialysis, anti- tumor necrosis factor (TNF), and organ transplants. For 90% of those who go on to develop TB disease, reactivation occurs within 2 years after the initial infection. Without effective detection and treatment of TB infection and disease, the chain of TB transmission will repeat. See Figure 2 for a summary of the natural history of TB.

[2] Davies P. The Natural History of Tuberculosis in Children. A Study of Child Contacts in the Brompton Hospital Child Contact Clinic from 1930 to 1952. Tubercle. 1961;42(Suppl).
[3] Starke JR, Jacobs RF, Jereb J. Resurgence of tuberculosis in children. The Journal of pediatrics. 1992;120(6):839-55.
[4] Bloom BR, Murray CJ. Tuberculosis: commentary on a reemergent killer. Science. 1992;257(5073):1055-64.
[5] Vynnycky E, Fine PE. Lifetime risks, incubation period, and serial interval of tuberculosis. American journal of epidemiology. 2000;152(3):247-63.
[6] Devadatta S, Dawson J, Fox W, Janardhanam B, Radhakrishna S, Ramakrishnan C, et al. Attack rate of tuberculosis in a 5-year period among close family contacts of tuberculous patients under domiciliary treatment with isoniazid plus PAS or isoniazid alone. Bulletin of the World Health Organization. 1970;42(3):337.

Figure 2:
Natural History of Tuberculosis



Difference between TB disease and Latent TB Infection

The table below distinguishes the clinical, bacteriological and radiological manifestations of LTBI versus TB disease.

Table 2: Difference between Latent TB Infection and TB disease

Characteristics	Tuberculous infection	Tuberculosis disease
Symptoms	None	Most present with one or more of the following symptoms: cough, weight loss, fever, night sweats, chest pain, haemoptysis, fatigue, and decreased appetite.
Tuberculin skin test or Interferon Gamma Release Assays (IGRA)	Usually Positive	Usually positive
Bacteriology	Negative	Respiratory specimens are usually positive on smear microscopy, Gx or culture. However, may be negative in persons with extrapulmonary disease or minimal or early pulmonary disease.
Chest radiograph	Normal	Usually abnormal
Infectiousness	No	Often infectious (before treatment)
Tuberculosis case	No	Yes
Preferred treatment	Preventive treatment	Tuberculosis treatment

Priority or targeted TPT groups

People with acquiring TB infection and developing TB disease are defined as priority target groups to receive TPT. These groups include:

- People living with HIV
- Household contacts of bacteriologically confirmed (BC) TB cases including children under 5 years old, children above 5 years old, adolescents and adults
- Within household contacts the following people are more vulnerable:
    - Children <5 years old
    - Adult >60 years old
    - Diabetes
    - Smoking
    - Chronic Kidney Disease with or without dialysis
    - Anti-TNF treatment
    - Transplantation (including candidate)
    - Substance abuse
    - Silicosis

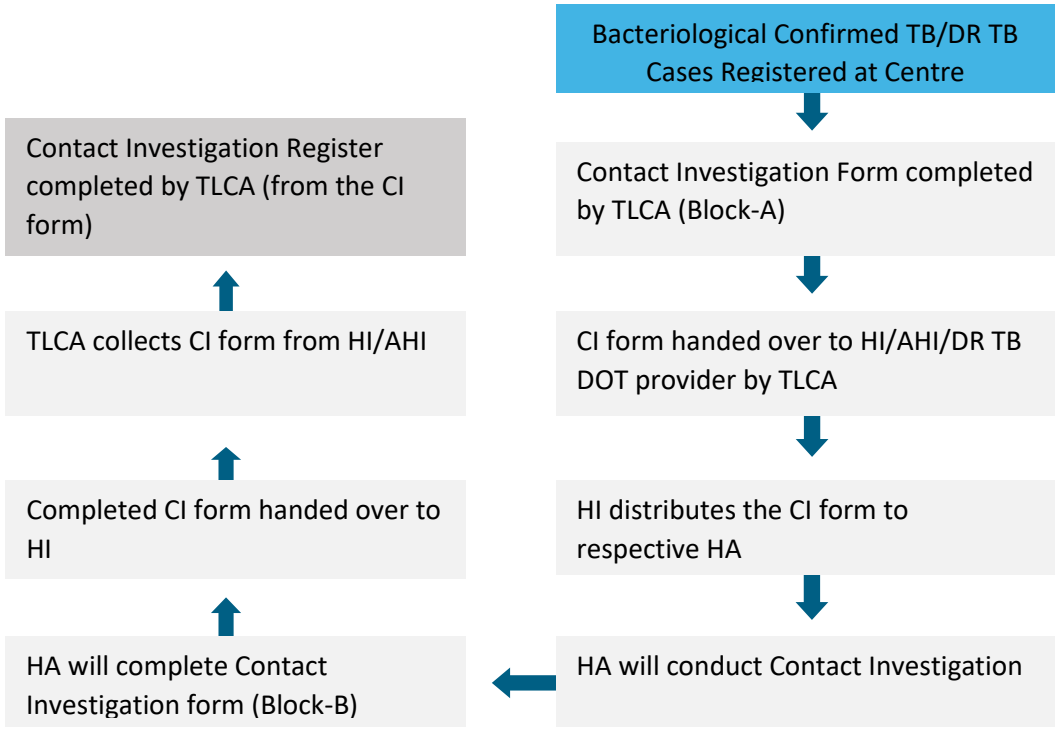
PROCEDURES TO IDENTIFY PERSONS POTENTIALLY ELIGIBLE FOR TPT

1. Contact investigation procedures

- The TB Leprosy Control Assistant (TLCA)/laboratory staff /DOT centre staff will interview the index BC-TB patient and record the details of contacts including name, age, sex, address and contact numbers in the CI Form for DS/DR TB (See Annex 1).
- The CI form is given to the (Health Inspector) HI who distributes the form to the relevant health assistant (HA) who will then conduct household visit for the index case.
- In the urban setting the respective manager/paramedic will fill in Block A of the form and then distribute it to the community health care worker (CHW)/ DOT provider.
- Facility staff should advise index TB patients that a health care worker will come and check on the health status of household members/close contacts related to TB.
- The responsible HA/CHW/DOT provider will visit the home of the Index Case to collect more information and complete the CI form for all close contacts. S/he will interview the Index Case and family members to identify contacts. S/he will conduct primary symptom screening of close contacts and refer all symptomatic (adult and children) to the respective government facility/ nongovernmental organization (NGO) clinics for further evaluation.
- Children <5 years old should be referred to health facility, regardless of TB signs and symptoms. If asymptomatic, they need TPT.
- Contacts with TB signs and symptoms should be referred promptly to health facility for further investigation of TB.
- Contacts without signs and symptoms of TB should also be referred to health facility for further investigation of LTBI and TPT.
- All contacts of DR-TB index cases should be referred to facility for evaluation.

- HA/CHW/DOT provider will issue a referral slip (see Annex 2) to contacts. Slips will be collected at the initial visit site and the number reported for inclusion in cascade evaluation.
- All contacts will be identified and evaluation will commence within 14 days after diagnosis of the index case.
- Completed CI Forms will be returned to HI and then to TLCA to complete CI registration book.
- TLCA's will ensure proper implementation, recording and reporting of CI.
- CI and TPT modules should be completed within e-TB manager. The data from the TPT form and register will be encoded in e-TB manager by the data clerk in the UHC as directed by the HI. Data completeness and accuracy will be checked monthly and quarterly. Quarterly analysis and reports on CI and TPT will be produced.
- See Figure 3 for graphic depiction of CI process from Bangladesh CI SOPs.

Figure 3. Contact Investigation Algorithm for contacts



2. Procedures during Active Case Finding in Community and Congregate Settings

TB infection investigation and TPT provision should be integrated into active case finding (ACF) among populations vulnerable to TB in community and congregate settings. TB infection investigation may be limited only to the household and close contacts of index TB cases identified in the ACF activities. Whenever an active TB is diagnosed during an ACF activity, immediately ask about household and close contacts and screen them for TB and TB infection. Targeted vulnerable groups for ACF activities include:

- Urban and rural poor communities as targeted by NTP

- Those living in congregate settings such as jails; prisons; homes for elderly, orphans, or persons with disabilities; detoxification centers; and evacuation shelters for internally displaced populations
- Targeted workforce including miners, construction workers, public transport drivers, garment factory workers, or any workplace where disease outbreak occurs

To prepare to conduct ACF and TPT activities in congregate settings and workplaces first:

- Obtain prior approval from relevant authorities and community leaders.
- Discuss and prepare strategies to address the stigma, confidentiality and privacy issues.
- Ensure the availability of required resources.
- Engage with all concerned stakeholders in proper planning including logistic, medical and laboratory supplies needed for the activity.
- Conduct proper training to staff undertaking combined ACF and TPT strategies.

PROCEDURE TO EXCLUDE ACTIVE TB DISEASE AND DECIDE ABOUT TPT

It is extremely important to exclude active TB disease prior to starting TPT for successful outcomes. The steps required to exclude active TB disease and decide about TPT are different depending on an individual's risk of developing TB disease. Figure 3 provides a summary algorithm for LTBI investigation and decision to provide TPT or not.

People at higher risk of developing TB disease

Those at higher risk of developing TB disease include:

- PLHIV
- Household contacts
    - <5 or ≥ 60 years old
    - Diabetics
    - Other clinical vulnerabilities
        - CKD with or without on dialysis
        - Anti-TNF treatment,
        - Transplantation (including candidate)
        - Silicosis
        - Smoking
        - Substance abuse

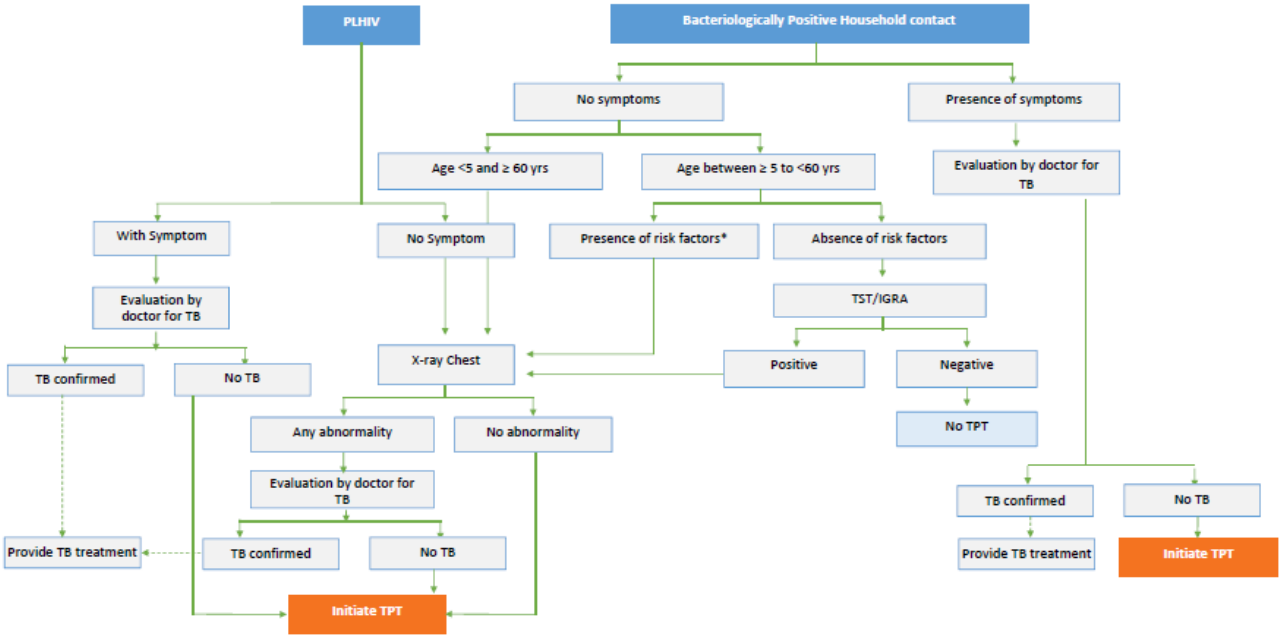
- TB signs and symptoms screening will be performed initially for these groups.
- TB signs and symptoms include cough for 2 weeks or longer, fever, weight loss and night sweats. In children <5 years old, additional features may be poor weight gain or failure to thrive (faltering weight curve), loss of appetite and lethargy (or reduced activeness).
- If one or more TB signs or symptoms is present, a doctor will evaluate the patient including complete laboratory diagnosis of TB (e.g. GeneXpert test) and investigation for other diseases at the discretion of the doctor.
- In the absence of TB signs and symptoms, Chest Xray (CxR) will be performed.

- If any abnormality suggestive of TB is identified, complete laboratory diagnosis of TB (e.g. GX) and investigation for other diseases will be done at the discretion of the doctor.
- If no abnormality is detected in the CxR, TPT will be provided.

People who are not at higher risk of developing TB disease

- Household contacts between 5 and 59 years of age without any risk factors are included in this category.
- A test for TB infection such as tuberculin skin test (TST) or Interferon-Gamma Release Assay (IGRA) will be performed in this group.
- If TST or IGRA is positive, a CxR will be taken.
- If any abnormality suggestive of TB is identified, laboratory diagnosis of TB (e.g. GX) and investigation for other diseases will be done at the discretion of the doctor.
- If no abnormality is detected in the CxR, TPT will be provided.
- If TST is negative, TPT will not be offered and discharge from contact investigation.

Figure 4: Algorithm for exclusion of active TB disease, LTBI testing and decision for TPT



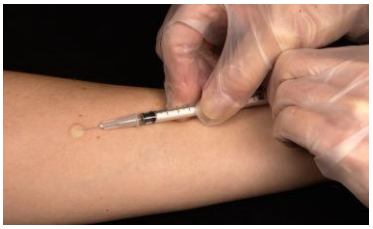
Risk factors:

- Diabetics
- Other clinical vulnerabilities
  - CKD with or without on dialysis
  - Anti-TNF treatment
  - Transplantation (including candidate)
  - Silicosis
- Smoking
- Substance abuse

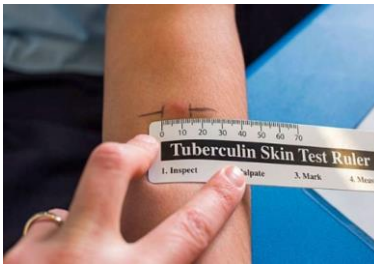
Performing Tuberculin Skin Test

Either 5-TU or 2-TU PPD can be used for TST. The test is performed by injecting 0.1 mL of PPD intradermally into the inner surface of the forearm with a tuberculin syringe, the needle bevel facing upward. If the injection is done correctly, it will produce a pale elevation of the skin (a wheal) from 6 to 10 mm in diameter. The skin reaction should be read between 48 and 72 hours and measured in millimeters of the induration (palpable, raised, hardened area or swelling) but not erythema (redness).

Correct PPD test with a wheal



Reading TST result



Source: CDC.gov

The diameter of the indurated area should be measured across the forearm (perpendicular to the long axis). The induration of ≥10 mm is considered a positive result generally, but ≥5 mm for those with immunocompromise such as severe malnutrition or advanced HIV.

Note: The NTP may introduce Interferon-Gamma Release Assay (IGRA) in the future. IGRA test measures the response of immune cells to simulated TB proteins when they are mixed with a small amount of whole blood. Currently there are two types of commercially available and WHO recommended IGRA tests: QuantiFERRON(R) TB Gold in Tube and T-SPOT(R) TB.

TPT REGIMENS

Table 4: Summary of TPT regimens recommended by WHO[7]

TPT regimen	How to administer TPT regimens
6H	Isoniazid (H) daily orally for 6 months (conventional regimen being used in the programs)
3HP	Isoniazid (H) and Rifapentine (P) orally weekly dose for 12 weeks/3 months *Note: not recommended for children under 2 years old and pregnant women as studies of rifapentine safety in these population groups have not done yet.*
3HR	Isoniazid (H) and Rifampicin (R) orally daily dose for 3 months
4R	Rifampicin (R) orally daily dose for 4 months*
1HP	Isoniazid (H) and Rifapentine (P) orally daily dose for 1 month

* 4R was not chosen as a regimen for Bangladesh, but may be useful for those with intolerance to isoniazid. See management of specific AEs below.

TPT REGIMEN OPTIONS IN BANGLADESH

Based on previous experience of TPT implementation in Bangladesh, specifically in under 5 children and PLHIV, Bangladesh has decided to use the following TPT regimens based on age groups and HIV status.

[7] https://www.who.int/publications/i/item/who-consolidated-guidelines-on-tuberculosis-module-1-prevention-tuberculosis-preventive-treatment

Table 5. TPT Regimen Options for Bangladesh

Age group	Regimen	Administration
≥15 years (including all adults without HIV)	3HP/ 3HR	Isoniazid (H) and Rifapentine (P) once per week administration for 3 months (12 doses in total)/ Daily administration of Isoniazid (H) and Rifampicin (R) orally for 90 days/3 months
<5 years	6H/ 3HR	Daily administration of isoniazid (H) for 6 months/ Daily administration of Isoniazid (H) and Rifampicin (R) orally for 90 days/3 months
Children from 5 to 15 years old	3HR	Daily administration of Isoniazid (H) and Rifampicin (R) orally for 90 days/3 months
PLHIV all ages	6H	Daily administration of Isoniazid (H) orally for 180 days/6 month

PREVENTIVE TREATMENT FOR CONTACTS OF MDR-TB CASES

Limitations of the quality of evidence prevent drawing any recommendations on multidrug-resistant TB (MDR-TB) TPT as a public health measure. Strict clinical observation and close monitoring of MDR-TB contacts for the development of active TB disease with 6 monthly follow-up for at least two years by signs and symptom screening is preferred over the provision of TPT for contacts with MDR-TB cases.

MDR-TB TPT

Selected high-risk household contacts of patients with MDR-TB may be considered for TPT based on individualized risk assessment and a sound clinical justification.

- MDR-TB TPT should be individualized after careful assessment of intensity of exposure, the certainty of the source case, reliable information on drug resistance pattern of source case and potential AEs.
- TPT should be given only to household contacts at high risk (e.g. children, people receiving immunosuppressive therapy, people with chronic disease (diabetes, CKD) and PLHIV).
- Drugs should be selected according to the drug susceptibility profile of the source case.
- Confirmation of LTBI tests with TPT or IGRA is required
- Strict clinical observation and close monitoring of MDR-TB contacts for the development of active TB disease for at least 2 years are required, regardless of the provision of TPT.

Adverse events related to TPT

Like any TB medications, the drugs used for TPT have similar potential adverse events. However, a study done by the NTP in collaboration with the Challenge TB project, with funding from the United States Agency for International Development (USAID) (February 2018 - May 2019) showed that it is safe to use the 3HP regimen among household contacts. Among 1,216 contacts who were enrolled in the study, 97% completed treatment through community based TPT. Of them 883 contacts of DS- TB patients over 2 years of age from 12 treatment centers in urban Dhaka were treated with 3HP regimen and adverse events were observed in 5% of them, with most of only mild severity.

Consider precautions for patients with increased risk for hepatotoxicity. This includes those with a history of liver disease, including chronic liver diseases (cirrhosis, hepatitis B or C, liver cancer), those regularly

using alcohol, pregnant or postpartum women (within 3 months) and those over 60 years of age. Monitor those at high risk for symptoms along with liver function tests monthly. Table 6 provides potential adverse events related to TPT.

Table 6. Potential Adverse Events of TPT Medications

TPT Medications	Known AEs	Rare AEs
Isoniazid	Asymptomatic elevation of liver enzymes Hepatitis Peripheral neuropathy Skin rash Sleepiness and lethargy	Convulsions Pellagra Arthralgia Anemia Lupoid reactions
Rifampicin	Gastrointestinal reactions (abdominal pain, nausea, vomiting) Hepatitis Generalized cutaneous reactions Thrombocytopenic purpura Discoloration of body fluids	Osteomalacia Pseudomembranous colitis Pseudoadrenal crisis Acute renal failure Shock Hemolytic anemia
Rifapentine	Gastrointestinal reactions (abdominal pain, nausea, vomiting) Hypersensitivity reactions (flu-like symptoms) Hepatitis Discoloration of body fluids	Hypotension/syncope Decrease in white blood cell and red blood cell count Decreased appetite Hyperbilirubinemia

Precautions for women of reproductive age (14 to 54 years old)

- Perform a pregnancy test, if needed (e.g., missed period).
- Ask women if they use contraceptives.
- **Advise women receiving oral contraceptives about taking rifapentine or rifampicin-containing regimens (i.e., 3HP, 3HR, 1HP and 4R) which can decrease the protective efficacy of contraception. They should either:**
    - **take an oral contraceptive pill containing a higher dose of estrogen (50 µ)** (e.g., Ogestrel ethinyl estradiol 50 mcg/ Norgestrel 0.5 mg**,** Ovcon-50 ethinyl estradiol 50 mcg/ Norethindrone 1 mg, Norinyl 1 + 50, Necon 1/50 Mestranol 50 mcg/ Norethindrone 1 mg**) or**
    - **use another form of contraception following consultation with a clinician.**
- Rifapentine should not be used for pregnant women.
- Precautions for **PLHIV** include the following:
    - Due to the cytochrome P450 isoenzyme inducing effect of rifamycin (rifapentine and rifampicin)-containing regimen, the blood concentration of some antiretrovirals (ARV) can be decreased so that drug levels are too low to work well.
    - Ask PLHIV which ARV they take and adjust if required (Table 7).

Table 7. Co-Administration of ART and Rifamycin-containing TPT Regimens (3HP, 3HR, 4R, 1HP)

Antiretrovirals	Can be co-administered with 3HP, 3HR, 4R or 1HP?
Efavirenz and Dolutegravir	Yes
Protease inhibitors (lopinavir, atazanavir, ritonavir) and Nevirapine	No, use 6H instead
Raltegravir	Yes, but increase raltegravir dose to 800 mg twice daily instead of usual dose of 400 mg twice daily

PREPARATION TO START TPT

Education and counseling for people eligible for TPT

- Educate about TB infection, TB disease, benefits of TPT and potential adverse events (AE) (see Annex 6: Education and counselling messages on adverse events)
- Agree on TPT delivery plan (e.g., through treatment partner, by family members, patient themselves).
- Counsel on adherence plan including:
    - Preferred time and day to ensure doses are remembered (e.g., in the early morning with a light meal every Friday).
    - If multiple family members are taking TPT, all family members set one time and remind each other.
    - Set an alarm clock or use a calendar with pop-up messages in mobile phone or smartwatch, or simply tick in a physical calendar.

Baseline assessment

- Perform baseline clinical examination focusing on underlying conditions that could increase the risk of AEs from TPT.
- Pregnancy test for women at reproductive age, if unsure of pregnancy status
- Baseline liver function test if risk factors for hepatotoxicity:
    - History of liver disease
    - Regular use of alcohol
    - Chronic liver disease (cirrhosis, hepatitis B or C, liver cancer)
    - Pregnancy
    - Within 3 months postpartum
    - Age >60 years
- Check age and HIV status to determine the TPT regimen to be given.
- Check body weight and prescribe the right dosage of TPT by following dosing in Table 8.
- Give pyridoxine (Vitamin B6) prophylactic dose for those on isoniazid containing regimen:
    - adults and children over 1 yr: pyridoxine 10 to 25 mg/day
    - Infants: pyridoxine 5-10 mg/day

Table 8: Dosing of TPT drugs with single formulations or fixed dose combinations (FDC)

Regimen	Dose by age and weight band				
6H (For PLHIV all age, for non-PLHIV <5 y.o)	Isoniazid	Age 10 years & older: 5 mg/kg/day Age <10 years: 10 mg/kg/day (range, 7–15 mg)			
3HR	Isoniazid	Age 10 years & older: 5 mg/kg/day Age <10 years: 10 mg/kg/day (range, 7–15 mg)			
	Rifampicin	Age 10 years & older: 10 mg/kg/day Age <10 years: 15 mg/kg/day (range, 10–20 mg)			
Weight band	4–7 kg	8–11 kg	12–15 kg	16–24 kg	>25 kg
RH 75/50 mg (FDC) Age ≤15 years	1	2	3	4	Use adult formulations *RH (150/75 mg)*
Weight band for adults	30–37 kg	38–54 kg	≥55 kg	-	
RH 150/75 mg (FDC) Age >15 years	2	3	4	-	*Maximum dose:* Isoniazid 300 mg Rifampicin 600 mg
3HP (once/wk for 12 wk)	≥15 years old				
Weight band	30–35 kg	36–45 kg	46–55 kg	56–70 kg	>70 kg
Isoniazid 300 mg	3	3	3	3	3
Rifapentine 150 mg	6	6	6	6	6
Isoniazid + rifapentine (FDC) (300 mg/300 mg)	3	3	3	3	3

CARE OF PEOPLE ON TPT

Regular follow-up of people on TPT

Conduct regular monthly follow-up. This does not need to be in person visits to health facility, but could instead by community visits or phone contacts. The following care should be provided:

- Educate about potential AEs.
- Agree on the follow-up plan, either in person at a health facility or in the community or by phone.
- Monitor body weight and AEs.
- Those with a high risk of hepatotoxicity or elevated baseline need monthly liver function tests (LFTs).
- Contact patient every month. For those unable to attend the clinic, this should be by community/home visit by CHW or by telephone (see checklist in Annex 7).
- Ensure continuous drug supply.
- Dispense for multiple months or even the whole course of TPT, especially for 3HP, 3HR. Dispense at least 2 to 3 months for longer regimens (i.e., 6H).
- Regularly screen and manage AEs.

- Correctly record and report as below.

Management of adverse events

It is important to regularly screen for AEs during regular follow-up in person or by phone when someone on TPT cannot come in (e.g. due to work, school schedule, or travel restrictions). The following are management strategies for each AE.

1. **Flu-like signs and symptoms**
   - Advise to stay hydrated by drinking plenty of water and juice.
   - Prescribe paracetamol 500 mg tid (3 times a day).
   - If severe and not tolerated, consider switching to an alternate regimen (6H)
2. **Nausea and vomiting**
   - Prescribe metoclopramide 10 mg bid (twice a day) or tid.
   - Advise to stay hydrated by drinking plenty of water and juice.
   - Avoid spicy and greasy food.
   - Prescribe oral rehydration solution, if there is mild dehydration.

3. **Hepatotoxicity**
   - If aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) are >3 but <5 times upper limit of normal (ULN) without signs and symptoms of hepatitis, continue TPT and repeat AST and ALT weekly.
   - If AST and/or ALT >3 times ULN with signs and symptoms of hepatitis or if AST and/or ALT >5 times ULN with or without signs and symptoms of hepatitis, stop TPT and do not reintroduce.
4. **Peripheral neuropathy**
   - Use brief peripheral neuropathy scoring system (BPNS) to screen and assess the severity of peripheral neuropathy.
   - If mild: give 100 to 150 mg of pyridoxine in adults and 50 mg in children.
   - If not better or worsens with an increased pyridoxine dose, stop H containing regimen and consider switching to 4R.
5. **Skin hypersensitivity reaction**
   - If itchiness and localized mild rashes occur, give calamine lotion or steroid cream to apply bid on affected area; chlorpheniramine 8 mg tid or bid orally may be given.
   - If itchiness, generalized rashes, or swelling of oral or nasal mucosa with or without fever, withhold TPT.
   - For mild or moderate hypersensitivity reaction, desensitization may be attempted with a low dose as is done for DS-TB treatment, once hypersensitivity reaction resolves to see if it was caused by isoniazid or rifapentine/rifampicin.
   - Never reintroduce after severe hypersensitivity reaction or Stevens-Johnson syndrome.
   - If it was caused by isoniazid, switch to 4R.
   - If it is caused by rifapentine, switch to 6H.
6. **Orange-red discoloration of body fluid (tear, saliva, urine, milk, urine)**
   - Reassure that it is just the staining from a drug in the regimen and is harmless. Advise to continue TPT.

7. **Any occurrence of TB signs and symptoms**
    - Investigate for active TB disease or other diseases.
    - If no active TB disease, continue TPT.
    - If active TB disease, stop TPT and provide DS-TB or DR-TB treatment, as appropriate.
8. **How to manage TPT regimen if switched for severe AE.**
    - For any regimen change, consult with national experts before switching to an alternate TPT regimen.
    - Prescribe the new regimen to continue for the proportion of time remaining to complete treatment.

An example of calculation of time remaining after switching TPT regimen for severe AE

A person who completes 3 doses of HP (i.e., 3 weeks), has finished 25% of 3HP regimen and needs 75% of the total doses to complete a full course of TPT. This is equivalent to 4.5 months (135 daily doses) of 6H regimen. Therefore, if this person switches from 3HP to 6H at 3 weeks, another 4.5 months of daily isoniazid is required after stopping 3HP.

Management of Missed TPT Doses or TPT Treatment Interruption

1. **3HP: Instruction to clients in case of missed dose**
    - Take the missed dose as soon as remembered and continue on as in the usual fixed schedule. For example, Client XX is taking TPT every Saturday for 3HP weekly regimen. But XX forgot the dose on Week 3 Saturday and remembered it on Monday. XX should take the missed dose now (Monday) for Week 3 and the usual Saturday dose continues from Week 4 onwards.
    - But if it is <72 hours before the next scheduled dose, just skip the missed dose and take the next one on schedule.
    - Extend treatment duration to make up for missed doses.
    - The extension should not be more than an additional 1 month for 3HP. If clients complete >80% of doses within the extended period, the treatment outcomes can be defined as "Treatment Completed".
2. **Daily regimens (6H and 3HR): Instruction to clients in case of missed dose**
    - Take the missed dose when remembered and continue longer to make up for the required doses within the maximum extended duration of the regimen that the client is taking.
    - Extend treatment duration to make up for missed doses.
    - The extension should not be more than 4 weeks for 3HR, 5 weeks for 4R and 2 months for 6H. If clients complete >80% of doses within the extended period, the treatment outcomes can be defined as **"Treatment Completed"**.

DEFINING TPT OUTCOMES

At the end of treatment, determine the outcome of TPT and record it in the TPT Treatment Card (Annex 3) and TPT Register (Annex 4).

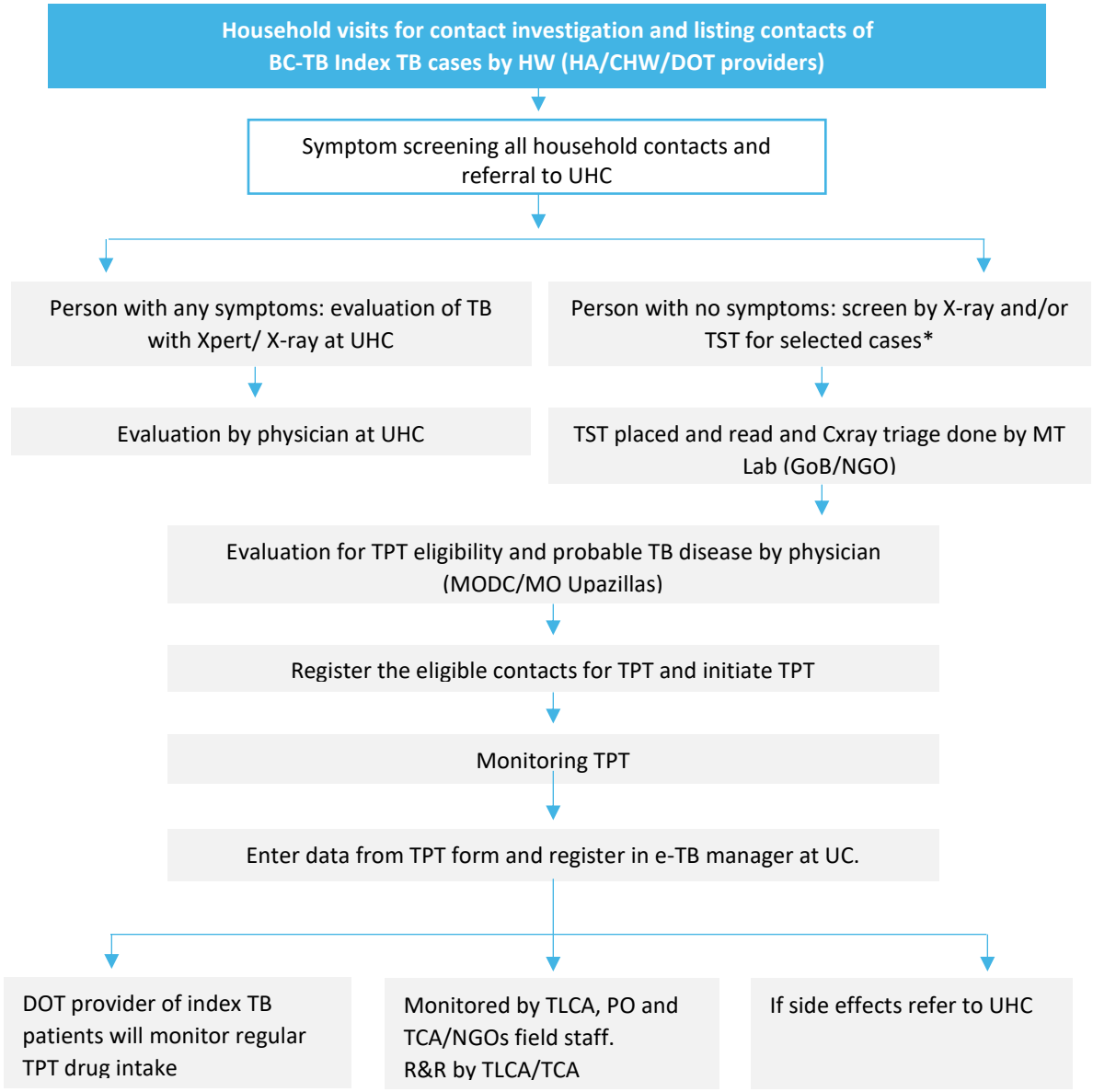
- *Completed* – an individual who has completed the prescribed duration of treatment and remains well or asymptomatic during the entire period.
- *Lost to follow-up* – an individual who interrupted TPT for 2 consecutive months or more for 6H, 4 consecutive weeks or more for 3HP or 3HR or 5 consecutive weeks or more for 4R.
- *Died* – an individual who dies for any reason during the course of therapy.
- *Failed* – an individual who developed active TB disease anytime while on TPT.
- *Not evaluated* – an individual who has been transferred to another health facility with a proper referral slip for the continuation of TPT and whose treatment outcome is not known; include here discontinued by a physician because the patient cannot tolerate (e.g., severe ADR) or those who refused to continue TPT.

IMPLEMENTATION STRATEGY FOR TPT AMONG HOUSEHOLD CONTACTS

- TLCA will give a list of households with index TB cases to health workers (HA/CHW/DOT providers) who will conduct contact tracing.
- Health workers will visit the household and enlist the household contacts and conduct TB screening by signs and symptoms.
- The contacts with TB signs and symptoms will be referred to UHC for further evaluation of TB by a physician including prescription of lab test for TB (i.e. GXpert test).

- The contacts without TB signs and symptoms will be referred for further evaluation on TPT eligibility by TPT and/or CxR by a physician at the UHC.
- Those eligible for TPT will have baseline evaluation and initiate TPT by a physician at the UHC.
- Persons started on TPT will be recorded in the TPT treatment card and in the TPT register.
- Monitoring and support to adherence to TPT will be done by DOT providers by checking adherence and adverse events.
- Person experienced adverse event will be promptly referred to UHC for further evaluation and management by a physician.
- An assignment of TPT outcomes will be decided and recorded by a physician in the UHC.
- Programmatic performance of TPT through recording and reporting and regular filed visit will be monitored and reviewed by TLCA.

Figure 5: Algorithm for TPT implementation strategy



DRUG AND CONSUMABLE SUPPLY AND MANAGEMENT

1. The supply and distribution of TPT drugs including TST reagents and other consumables (syringes, needle for TST, etc.,) will use the same mechanisms and arrangements as DS TB.
2. A purchase order will be completed by the central NTP and supplies stored at the NTP Central Warehouse at Shyamoli.
3. Quarterly distribution from central store to peripheral district store or district/upazila/urban DOTS centre will be done together with the 1st-line TB drug supply. As required, the cold chain will be maintained throughout the supply chain for TST reagents.
4. TPT drugs and TST reagents will be stored under proper conditions as below:
   - Store in cool, dry, ventilated and secured conditions, away from direct sunlight.
   - Ensure optimal temperature conditions for drugs and TST (refrigeration at 2-8 degree Celsius) within the required specified temperature range for the products.
   - Measure temperature 3 times per day and record in the temperature chart.
5. The inventory will be managed properly to avoid over or understock or treatment interruption for TPT. Inventory management includes:
   - Update the inventory every time a store receives or issues any item.
   - Monthly inventory update including month-end balance verified through physical count.
   - Share the inventory data with NTP PSM at the end of each month.
   - CWH (Shyamoli) will use electronic tool named “TB WIMS” as the inventory management information system.
   - In peripheral drug stores inventory management will be manual/paper-based.

SUPERVISION AND MONITORING

Supervision and monitoring of overall TPT program performance at both national, district and facility level will help improve quality of TPT services.

- The NTP will routinely evaluate the TPT program and design interventions through reviewing the data and reports, as well as integrating TPT components into supervisory visits conducted for DS-TB to help improve performance.
- At field level, the Upazilla Health Family Planning Officer (UHFPO) will be responsible for ensuring proper implementation, recording and reporting of TPT. S/he will review regular implementation updates, analyze reports and use data for TPT program improvement.
- HA, HI, AHI, DOTS providers and TLCA will coordinate on the various steps including, timely visits to index clients at home, referral of symptomatic cases (adult and children) for TB diagnostics and referral of all asymptomatic contacts for evaluation and possible TPT.

RECORDING AND REPORTING

- Data from CI and TPT will be collected in standardized forms and registers (see Annexes 1 through 5), and the reporting flow will be the same as in DS-TB.

Annex 1: Contact Investigation Form: After recording the details of contacts this form will guide household visits for contact investigations and will be used to collect information on all close contacts.

Annex 2: Referral Slip: This will be issued at the time of home visit to refer contacts to health facilities for further evaluation.

Annex 3: TPT Treatment Card: to record individual information from the time of TPT initiation until the person is discharged by the TPT service providers (doctors/nurses) at health facilities

Annex 4: TPT register: is a TPT master register and to utilize for cumulative and summary recording of anyone enrolled on TPT by the health facilities for easy analysis quarterly

- Annex 5: TPT reporting form: is a quarterly summary TPT performance reporting form to be completed by TLCA through a case-based monitoring system: a customized DHIS2 LTBI application.
- The NTP will also explore the option of integrating the LTBI application with eTB Manager.

The NTP will engage with other implementing

- All beneficiaries will be notified to NTP and monitored partners to develop digital solutions in the LTBI treatment adherence monitoring process.
- Periodic quarterly cohort reports will be generated for analysis by NTP to help monitor program performance.
- Monitoring indicators are provided in Table 9 below.

Table 9: Monitoring indicators for TPT activities

Indicator	Numerator	Denominator	Data source	Level
Proportion of contacts under 5 years initiated on TPT after ruling out TB	Number of contacts under 5 years initiated on TPT	Number of contacts under 5 years with TB ruled out during the quarter	CI register	Health facility, district, regional, national
Proportion of contacts aged 5 years and above initiated on TPT after ruling out TB	Number of contacts aged 5 years and above initiated on TPT	Number of contacts aged 5 years and above ruled out TB during the quarter	CI register	Health facility, district, regional, national
Proportion of contacts under 5 years completed TPT	Number of contacts under 5 years completed TPT	Number of contacts under 5 years initiated on TPT 6-9 months ago	TPT register	Health Facility, District, regional, national
Proportion of contacts aged 5 years and above completed TPT	Number of contacts aged 5 years and above completed TPT	Number of HHCs aged 5 years and above initiated on TPT 6-9 months ago	TPT register	Health facility, district, regional, national
Proportion of contacts under 5 years detected with TB while on TPT	Number of contacts under 5 years detected with TB while on TPT	Number of contacts under 5 years initiated on TPT 6-9 months ago	TPT register	Health facility, district, regional, national

Proportion of contacts aged 5 years and above detected with TB while on TPT	Number of contacts aged 5 years and above detected with TB while on TPT	Number of contacts aged 5 years and above initiated on TPT 6-9 months ago	TPT register	Health facility, district, regional, national
Proportion of contacts s under 5 years stopped TPT due to ADR	Number of contacts under 5 years stopped TPT due to ADR	Number of contacts under 5 years initiated on TPT 3-6 months ago	TPT register	Health facility, district, regional, national
Proportion of contacts aged 5 years and above stopped TPT due to ADR	Number of contacts aged 5 years and above stopped TPT due to ADR	Number of contacts aged 5 years and above initiated on TPT 3-6 months ago	TPT register	Health facility, district, regional, national
Proportion of newly detected PLHIV initiating TPT after ruling out TB	Number of PLHIV initiating TPT	Number of PLHIV detected during the quarter	ART/register	Health facility, district, regional, national
Proportion of newly detected PLHIV completing TPT	Number of PLHIV completing TPT	Number of PLHIV initiated on TPT 6-9 months ago	ART/register	Health facility, district, regional, national
Proportion of PLHIV who stopped TPT due to ADR	Number of PLHIV who stopped TPT due to ADR	Number of HHCs aged 5 years and above initiated on TPT 3-6 months ago	ART/ register	Health facility, district, regional, national

REFERENCES

- Expansion plan for tuberculosis preventive therapy in Bangladesh, NTP, 2020
- Revised national tuberculosis guidelines, draft, 2020
- WHO consolidated guides on tuberculosis, Module 1: Prevention – TB preventive Treatment, 2020
- WHO operational handbook on tuberculosis, Module 1: Prevention - TB Preventive Treatment, 2020
- INH and Rifapentine Treatment for LTBI: Expert Opinions About 3HP Utilization, March 17, 2016 Curry International Tuberculosis Center accessed at 3HP webinar materials | Curry International Tuberculosis Center (ucsf.edu)

ANNEX 1: CONTACT INVESTIGATION FORM

National Tuberculosis Control Programme-Bangladesh
Directorate General of Health Services
Contact Investigation (CI) Form for DS/DR TB

Date of Visit:_____

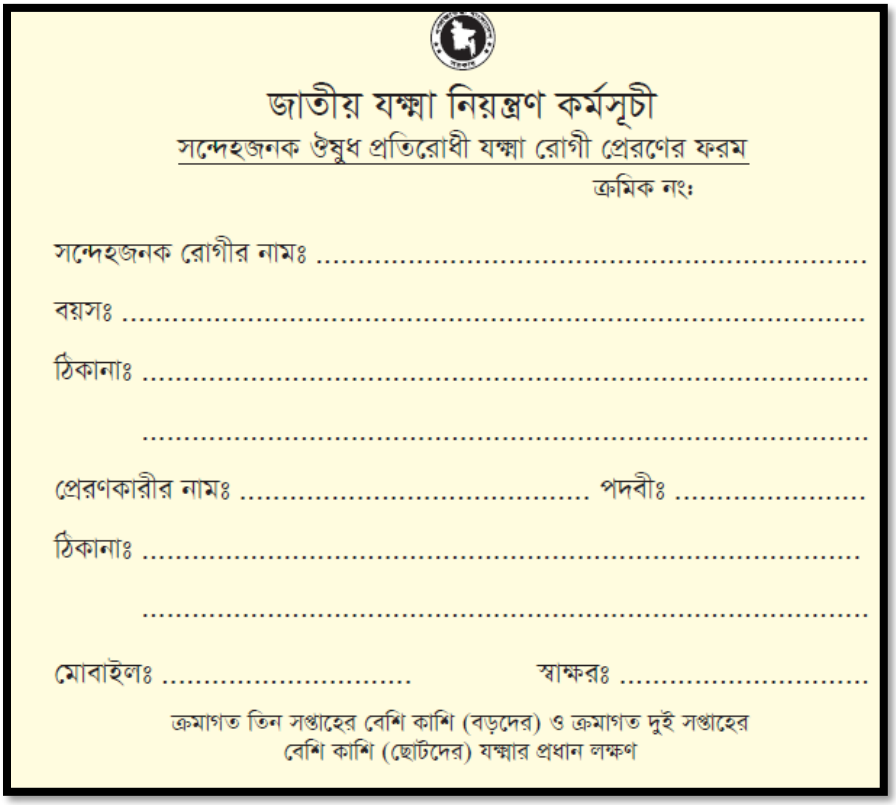
Block:A			
Information of Index Patient		Name of the DOTS Corner/DR TB Treatment Center	
Name		Treatment Initiation Centre	
Village/Ward		DS/DR TB registration number	
Union		Name of the Contact Investigator	
Upazila		Phone number of contact investigator	
District		Name of the DOT provider	
Division		Designation of the DOT provider	
Phone Number		Phone number of the DOT provider	

Block:B								
Sl. No.	**Contact Name**	**Age (Y/M)**	**Sex M/F/Others**	**Relation Code ***	**Symptoms Code****	**Refer Yes/No**	**Outcome Code*****	**Remarks**

*Relation Code: 1. Household member, 2. Workplace member, 3. Neighbour, 4. Others
**Symptoms code: 1. Cough for 2 weeks, 2. Fever, 3. Weight loss, 4. Cough with blood
For Child: 1. Cough for 2 weeks, 2. Fever, 3. No significant weight gain, 4. Cough with blood, 5. Lethargy
***Outcome code: 1. DS TB, 2. Healthy, 3. Other disease, 4. Eligible for TPT/IPT, 5. Did not come

Signature

ANNEX 2: REFERRAL SLIP



জাতীয় যক্ষ্মা নিয়ন্ত্রণ কর্মসূচী

সন্দেহজনক ঔষুধ প্রতিরোধী যক্ষ্মা রোগী প্রেরণের ফরম

ক্রমিক নং:

সন্দেহজনক রোগীর নামঃ .....

বয়সঃ .....

ঠিকানাঃ .....

.....

প্রেরণকারীর নামঃ ..... পদবীঃ .....

ঠিকানাঃ .....

.....

মোবাইলঃ ..... স্বাক্ষরঃ .....

ক্রমাগত তিন সপ্তাহের বেশি কাশি (বড়দের) ও ক্রমাগত দুই সপ্তাহের বেশি কাশি (ছোটদের) যক্ষ্মার প্রধান লক্ষণ

ANNEX 3: TB PREVENTIVE TREATMENT (TPT) CARD

National Tuberculosis Control Programme
Directorate General of Health Services, Bangladesh

TB Preventive Treatment (TPT) Card

Name of the eligible person: ---------- ----------Age: ___ Year Month _____ Sex: □ M □ F BCG Scar: □ Yes □ No

Father's Name: ---------- ----------Mother's Name: _____ _____

Address:----------Upazila/Ward/CC: _____ District:_____Phone no: _____

TPT Registration no: ----------Date: _____ TB Registration no. of source case:_____Date: _____

Relation with the source case: _____ Health Institution/DOT center: _____

Name, address and Ph no. of TPT Provider/Supervisor: _____

Month	Date	Weight/(kg)	No. of tablet* (H/3HR/3HP)	Date of next visit	Clinical evaluation**
0					
1					
2					
3					
4					
5					
6					

* Dose of INH: 10mg/kg body weight/day

** If symptoms of TB appear, refer to a Medical Doctor

Remarks: _____

_____

_____
Signature of Medical Officer

ANNEX 4. TB PREVENTIVE TREATMENT (TPT) REGISTER

National Tuberculosis Control Programme

Directorate General of Health Services, Bangladesh

TB Preventive Therapy (TPT) Register

Date	Name of *Eligible person	Age		Sex (M/F)	Name and address of Parents	TB Registration no. of source case	Relation with source case	**TPT Registration no.	TPT Registration date	TPT Regimen		TPT starting date	TPT completion date	***Outcomes	Remarks
		Year	Month							3RH/H	3HP				

***Eligible for TPT:**

1. Household/Close contact with pulmonary bacteriologically confirmed TB patient who has no active TB disease

****TPT Registration number:** This number will be for eligible person for TPT

*****Outcomes:**

1. Preventive treatment completed: Full course of TPT completed (3/6 months)
2. Monitor any adverse effects during the course of TPT

ANNEX 5: QUARTERLY TPT ACTIVITY REPORT FORM

TB 15

NATIONAL TUBERCULOSIS CONTROL PROGRAM

Directorate General of Health Services, Bangladesh

Quarterly TPT Activities Report of Tuberculosis

Name of District: Name of Upazila/ Centre/ Address: Name & Signature of UH&FPO/ In-charge of DOTS/ Health Unit:	Case registered during				Date of Completion of this Form: Name, Designation, Signature & Contact no. of Person completed the Form:
		quarter		Year	

No. of eligible for TPT			No. registered for TPT		
Male	Female	Total	Male	Female	Total

Age-groups (eligible for TPT)							
<5 years (3HR/H)		5 to less than 10 years (3HR)		10 to less than 15 years (3HR)		15 years and above (3HP)	
Male	Female	Male	Female	Male	Female	Male	Female

Age-groups (registered for TPT)							
<5 years (3HR/H)		5 to less than 10 years (3HR)		10 to less than 15 years (3HR)		15 years and above (3HP)	
Male	Female	Male	Female	Male	Female	Male	Female

No. of eligible for TPT (PLHIV)			No. registered for TPT (PLHIV)		
Male	Female	Total	Male	Female	Total

ANNEX 6: EDUCATION AND COUNSELLING MESSAGES FOR TPT

What is latent TB infection?

"TB" is short for a disease called tuberculosis caused by TB germs. TB is spread through the air from one person to another. People who become infected with TB germs but do not feel sick have what is called latent TB infection (LTBI). The reason a person does not feel sick is that the TB germs are latent or inactive (sleeping) in their body. A person with LTBI has no symptoms and cannot spread TB germs to others.

Why take treatment for LTBI?

A person with LTBI can have TB germs in their body for years before getting sick.

Taking TB preventive medicine is the only way to kill TB germs in your body.

Taking TB preventive medicine can prevent you from having TB disease in the future.

What are the medicines that you will take for 12 weeks?

You will take two medicines (rifapentine and isoniazid) once a week for twelve weeks. You will either meet a community health worker to assist you in taking your medicine, or you may take these medicines on your own.

One of the drugs, isoniazid, may cause tingling or numbness in hands and feet. Your doctor may add vitamin B6 to your treatment plan to prevent this after assessing you for pre-existing conditions.

Before you start this treatment plan, tell your doctor if you are taking any other medicines, including birth control medications and medicine for HIV. Isoniazid and rifapentine may interact with certain medications, so your doctor needs to know what medicines you are taking.

If you seek healthcare somewhere else (private clinic, drug store..), be sure to tell the provider that you are being treated for LTBI.

We would like to inform you about the possible side effects of TPT, although such side effects are not common. If these occur, they are usually mild and resolve spontaneously or with symptomatic treatment for a few days without needing to stop TPT. We are informing you of these possible side effects so that you can let us know if they occur, then we will be able to advise you on what to do and provide the necessary management of side effects. Please do not stop TPT without consultation with your health care provider. The possible side effects include the following:

- Fever
- Nausea and vomiting
- Loss of appetite
- Brown- or orange-colored urine (color of coffee or cola)
- Yellow skin or eyes
- Tiredness or weakness lasting 3 or more days
- Abdominal tenderness
- Easy bruising or bleeding
- Itchiness or rashes

- Numbness and tingling in hands or feet
- Joint pains

If you have any of these, report to your health worker. Your health worker will also check with you about any side effects.

If you get sick with a cough, unexplained fever, unexplained weight loss, and night sweats, please inform your health worker so that you can be assessed by a doctor to exclude active TB disease. It is extremely unlikely to develop active TB disease while you are on TPT provided that you are taking TPT medication regularly with correct dosage as prescribed by the doctor.

Take your medication: every dose matters.

Schedule a day and time to take your medicine. Use these tips to help you remember:

- Use a medication tracker or calendar to check off the days you have taken your medicine.
- Set an alarm for the time you need to take your medicine.
- Write yourself a note as a reminder to take your medicine. Put it in a place where you can easily see it, like on your closet door, bedroom door, bathroom mirror, or on your refrigerator.
- Ask a family member or friend to help you remember.
- Take your pills after eating. Eating before taking your medicine helps your body absorb the pills better.
- You will need to swallow all the pills in one sitting within 5 to 10 minutes.

If you forget to take your pills, call your doctor or clinic right away.

Your health worker will also check with you about missed doses.

Store your pills.

- Keep the medicine at room temperature.
- Keep the rifapentine pills in the blister pack until you are ready to take them.
- Store your medicine away from children.
- Keep your medicine in one place where you cannot miss it.

Limit alcohol use.

Alcohol use is associated with an increased risk of liver damage when taking isoniazid.

You should discuss drinking alcohol with your doctor before starting your medicine.

Side Effects

- It is normal if your urine (pee), saliva, tears, or sweat becomes orange-red colored.
- Isoniazid may cause tingling or numbness in hands and feet. Your doctor may add vitamin B6 to your treatment plan to prevent this.
- Review the checklist of signs and symptoms that may develop if your body does not tolerate this treatment.
- People react differently to medicines. If you are having any reaction to your treatment, stop taking your medicine and call your doctor or nurse right away!

Women

This medication may interfere with hormone-based birth control (including birth control pills, rings, and shots).

During treatment, non-hormonal barrier forms of birth control (intrauterine device or condoms) should be used to avoid pregnancy. Consult with your clinician if you are using hormonal contraception, which may need to be changed to one that contains a higher dose of estrogen.

If you become pregnant while on 3HP regimen, stop taking your medicine and speak with your doctor or nurse.

How to take your TPT medicine?

Follow the instructions below for your specific regimen.

3HP Regimen

- To treat your LTBI with 3HP, take two medicines (rifapentine and isoniazid) once a week for 12 weeks. It is essential to take all of your medications.
- The 12-dose regimen is not recommended for children <2 years old, pregnant women, or women who expect to become pregnant during treatment, or some persons taking medicine for HIV.

3HR Regimen

- To treat your LTBI with 3HR, take two medicines (rifampicin and isoniazid) daily for 3 months. It is essential to take all of your medications during the entire course of treatment.

6H Regimen

- To treat your LTBI with 6H, take one medicine (isoniazid) daily for 6 months. It is essential to take all of your medications during the entire course of treatment.

ANNEX 7: CHECKLIST FOR MONTHLY SCREENING ON ADVERSE EVENTS

Name or Initial of person on TPT: _____ Index TB No.: _____
To be completed in person or by phone. Tick in the box if any AEs. If none, no need to fill this sheet.

See table on next page for details of symptoms and management recommendations.

AEs	AE Started Date	Management Given	Resolved Date
☐ Flu-like signs and symptoms			
☐ Nausea and vomiting			
☐ Hepatoxicity			
☐ Peripheral neuropathy			
☐ Skin hypersensitivity reaction			
☐ Occurrence of TB signs and symptoms			
☐ Others (specify)			

Was regimen withheld: ☐ Yes ☐ No; if **Yes**, indicate date: _____

Was the regimen switched? ☐ Yes ☐ No; if **Yes**, indicate date: _____

If switched, which regimen was started:_____

Was TPT completely stopped due to AEs? ☐ Yes ☐ No; if **Yes**, indicate date: _____

Who decided to stop TPT completely? ☐ Doctor ☐ Other HCW ☐ Client

Other information:_____

Checklist for monthly screening on adverse events

Symptoms	Actions
Flu-like signs and symptoms: Fever, headache, runny nose, joint pain, etc	If mild, advise to take plenty of water and paracetamol, if required Can resolve spontaneously Continue TPT Advise to come immediately to a health facility if not tolerating or severe symptoms
Nausea and vomiting	Take TPT with meal Usually disappears after two weeks of starting TPT Advise to come to a health facility if not tolerating
Hepatotoxicity signs and symptoms: nausea, vomiting, loss of appetite, easy tiredness, abdominal pain, and yellow coloration of eye and skin	Advise to come to a health facility immediately for proper management Remind to come for regular follow up LFT to those with hepatotoxicity risk factors such as chronic hepatitis, alcoholic, other underlying liver disease or have abnormal baseline LFT
Peripheral neuropathy: Burning sensation, tingling, and numbness in the feet and/or hands	Advise to go to a health facility immediately for clinical examination and management
Skin hypersensitivity reaction	If itchiness and localized mild rashes, apply calamine lotion or steroid cream if required If itchiness, generalized rashes, swelling of lip or nosal mucosas, and fever: advise to come to a health facility immediately for proper management
Orange-red discoloration of body fluid (tear, saliva, urine, milk, urine)	Reassure that it is just the staining from a drug in the regimen (rifamycin group) and harmless, advice to continue TPT
Any occurrence of TB signs and symptoms (cough, fever, weight loss, night sweat)	Advise to come to a health facility for proper clinical follow-up