STANDARD NURSE PROTOCOLS FOR TUBERCULOSIS

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STANDARD NURSE PROTOCOL FOR ACTIVE TUBERCULOSIS (TB) DISEASE AGE 15 AND OVER

DEFINITION

Tuberculosis (TB) is an infectious disease transmitted through the air in droplet nuclei that are produced when a person with active TB disease of the lung or larynx sneezes, coughs, speaks, or sings. Persons breathing air contaminated with these droplet nuclei may become infected with TB.

Generally, a positive culture or positive Nucleic Acid Amplification test (NAAT) for *Mycobacterium tuberculosis* is necessary to confirm the diagnosis of TB disease. However, people being evaluated for TB may be diagnosed based on: a positive sputum/specimen smear for acid-fast bacilli (AFB); lung histology showing necrotizing granulomas with or without AFB; or clinical syndrome, even when a culture or pathologic specimen has not been, or cannot be obtained.

ETIOLOGY

Causative agent of TB is the *Mycobacterium tuberculosis* (*M.tb*) complex (*M. tuberculosis, M. bovis, M. africanum, M. microti, M. canetii, M. caprae, M.mungi and M. pinnipedii)*.

SUBJECTIVE

1. May have history of exposure to a known person with TB disease

2. May have history of active TB disease or latent TB infection

3. May have one or more of the following symptoms related to TB:

    a. Productive, prolonged cough (usually more than two- or three-weeks' duration)
    b. Fever
    c. Chest pain or pleuritic pain
    d. Chills
    e. Night sweats
    f. Easily fatigued
    g. Loss of appetite
    h. Weight loss without dieting
    i. Hemoptysis (coughing up blood)
    j. Headache
    k. Muscle/bone/joint pain

    NOTE: A complete medical history and review of current medications is required to determine if there are any

diseases/illnesses present that would require consultation or referral to delegating physician.

OBJECTIVE Physical examination performed per guidelines may reveal the following criteria that are useful in identifying a person with TB disease:

1. Coughing or shortness of breath
2. Fever/sweating
3. Appears ill or fragile
4. Vital signs (height, weight, BMI, blood pressure, respiratory rate)
5. Jaundice of sclera or skin
6. Abdominal tenderness
7. Joint swelling or redness
8. Difficulty walking, tremors
9. Dizziness, syncope, memory loss

ASSESSMENT

1. Pulmonary tuberculosis

OR

2. Extra-pulmonary tuberculosis

OR

3. Person being evaluated for pulmonary tuberculosis

OR

4. Person being evaluated for extra-pulmonary tuberculosis

For patients with the following conditions, consultation with the delegating physician is required for patients to be treated under this protocol. Consultation must be documented in the patient's record.

1. BMI greater than 30 (obese)

2. BMI lower than 17 (underweight)

3. Age greater than 75 years old

4. Diabetes mellitus

5. Pregnant/breastfeeding

6. Liver disease

7. Extra-pulmonary TB not requiring 2nd line TB drugs or use of corticosteroid therapy (Excludes: Central Nervous System (CNS) TB, TB pericarditis: these cases must be referred for physician management.)

8. Allergic reactions not requiring 2nd line TB drugs

9. Decision to extend continuation phase using first-line TB drugs, e.g., bone/joint TB, miliary TB

10. Review of current medications reveal potential for drug-drug interactions with TB medications

11. Treatment interruptions:

    a. During the initial phase of treatment if the lapse is 14 days or more in duration
    b. During the continuation phase of treatment:
        1) If patient is smear positive initially and received less than 80% of the planned total doses for continuation phase
        2) Any patient whose lapse is 3 months or more in duration combined or a lapse of 2 consecutive months

NOTE: For patients with the following conditions, referral to the delegating physician is required and patients cannot be treated under this protocol:

1. TB treatment for children **from birth up to 15 years of age (i.e., age 0 – 14 years)**

2. Any known drug resistance to anti-TB medications

3. Known HIV infection

4. Central Nervous System (CNS) TB

5. TB pericarditis

6. TB patient requiring adjunctive use of corticosteroid therapy

7. Use of once-weekly Isoniazid and Rifapentine in continuation phase for active TB disease

8. Renal insufficiency **(**estimated creatinine clearance less than 70 mL/ min**)**

9. End-stage renal disease on hemodialysis

10. Any TB patient requiring 2nd line TB drugs

11. Treatment failure (positive culture of *M. tuberculosis* after 4 months of treatment)

12. Suspected TB meningitis

PLAN

The desired outcomes of treatment of active TB disease are biologic cure, prevention of drug resistant TB and prevention of transmission of TB to individuals exposed to persons with active TB.

NOTE: Any hospital admissions or deaths of persons with TB disease are to be reported immediately to the **District TB Coordinator who in turn will report to the State TB Office.**

INITIAL DIAGNOSTIC STUDIES

1. If positive results for either an IGRA or a TST cannot be verified (including millimeters [mm] of induration), perform a TST or IGRA. **An IGRA is the preferred method of testing in individuals 2 years of age and older who are foreign born and/or have a history of BCG vaccination. TB skin testing should be performed on children less than 2 years of age.** Vaccination with live viruses may interfere with either of these test reactions. For persons scheduled to receive a TST **or IGRA,** testing should be done as follows:

a. Either on the same day as vaccination with live-virus vaccine

OR

b. 4-6 weeks after the administration of the live-virus vaccine, at least one month after smallpox vaccination

2. Collect three sputum specimens on consecutive days for culture **per procedure for spontaneous sputum collection for TB. Identify patients with dry, non-productive cough for nebulized sputum induction. Follow guidelines for both spontaneous and nebulized sputum in the TB Policy & Procedure Manual, current version. Send specimen collected** to the Georgia Public Health Laboratory (GPHL) in Decatur.

   Use the lab slip found on the GPHL website at **http://dph.georgia.gov/lab.** Look at the related files at the bottom of the page for the GPHL Submission Form. Check *Smear, Culture, and Sensitivity* for all three specimens and *NAAT* for the first specimen only. Do not mark "smear only" unless the patient has had a recent positive culture result.

   The public health nurse (PHN) **or designee** will obtain the first sputum specimen and provide the patient with two additional containers for collection. Instructions should be given to both patient and family on how to properly produce sputum for examinations. At least one of the specimens collected MUST be an early morning specimen as they provide the highest yield for detecting *M.tb*. Ideally the initial specimens should be collected over a three-day period, however multiple samples may be collected in the same day if eight hours has elapsed between collections and at least one is an early morning specimen.

   Specimens **not picked up** the day of collection should be refrigerated. If necessary, the PHN **or designee** should collect, **transport or** mail the specimens. Optimum sputum specimens contain an 8-10 ml sample; however, any amount collected will be tested at the state lab. Specimens received by the lab that contain less than a 0.5 ml sample may have an insufficient quantity of material for all lab testing to be performed.

3. Perform the following baseline blood chemistry labs:

    a. Obtain aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin**,** alkaline phosphatase, CBC with platelet count, serum creatinine, **HgbA1C**, and Hepatitis C antibody for all adults.

Normal HgbA1C	**Below 5.6%**
Pre-Diabetes (HgbA1C)	**5.7% - 6.4%**
Diabetes (HgbA1C)	**6.5% or greater**

    NOTE: If HgbA1C is elevated between 5.6% and 6.4%, refer to Nutritionist or Primary Care Physician for prediabetes education and counseling. If HgbA1C is 6.5% or greater, refer patient to PCP for evaluation and follow up.

    NOTE: If Hepatitis C Ab is positive, refer patient to PCP for evaluation and follow up.

    b. Hepatitis B profile **(HBsAg, HBsAb, HBcAb)** should be obtained for all adults (regardless of birth country) and anyone less than 18 years old who is foreign-born.

    NOTE: If HBsAg is positive, refer to PCP for evaluation and consideration for treatment. If all HB serology results are negative (i.e., the patient is susceptible to Hepatitis B infection), consider Hepatitis B immunization as per ACIP guidelines.

    c. All individuals will be tested for HIV using the opt-out approach. Consent is inferred unless patient declines testing. If HIV positive, collaborate with HIV Program to obtain CD4 T-cell count, then refer to consulting physician.

4. Obtain baseline visual acuity testing and red/green color discrimination for patients being placed on Ethambutol.

5. **Perform a urine pregnancy test, if woman is of childbearing age.**

6. Refer patient to have chest x-ray performed to detect abnormalities compatible with TB disease.

DIAGNOSTIC STUDIES' FINDINGS

1. A positive interferon gamma release assay (IGRA) or a positive tuberculin skin test (TST). The absence of a positive IGRA/TST does not rule out the diagnosis of TB disease or latent TB infection, **particularly in immune compromised patients. Online link: https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-opportunistic-infection/325/tb**

2. Positive staining of AFB in sputum, bronchial brush, bronchial wash or lung tissue biopsy. However, a person with TB disease can be smear negative.

3. Chest x-ray showing abnormalities compatible with TB disease. (Radiographic findings of healed, inactive TB and reactivating TB sometimes cannot be distinguished). **See opportunistic infections: https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-opportunistic-infection/325/tb**

4. The following criteria (one or more) are required for a confirmed diagnosis of TB:

    a. Pathology findings compatible with the diagnosis of TB.
    b. Specimens with positive culture or positive NAAT for *M.tb.*

THERAPEUTIC

PHARMACOLOGIC

NOTE: Order medications for treatment with directly observed therapy (DOT) from drug stock and send a copy of the drug order(s) to the District Pharmacist or District Drug Coordinator. Refer to Tables 1 and 2 for options and dosages.

1. If a patient is REFERRED to the delegating physician for management, the PHN may not dispense ANY of the prescribed medications**.**

2. **PHN may not order or dispense 2nd line TB medications. Referral to the delegating physician and TB program Medical Consultant is required. Follow guidelines for ordering 2nd Line Therapy Authorization, Form is available at https://dph.georgia.gov/tb-public-health-clinic-forms**

Options for Dispensing of a Physician or Practitioner's Drug Order or Prescription:

The Prescribing Physician that meets the Dispensing Practitioner requirements of the Georgia Composite Medical Board can dispense the drugs. The Prescribing Physician may send the prescription to the District Pharmacist or a pharmacy by phone call or E-Scribe. A physician cannot dispense another practitioner's orders

3. **Video direct observed therapy (VDOT)**

Carefully selected patients meeting established minimum criteria may be eligible to receive their medications via VDOT. In order to perform VDOT the healthcare worker observes the patient take their medication via smartphone, laptop, or desktop. See Tuberculosis Policy and Procedure Manual for additional information.

Table 1: Regimen Options - Treatment of Patients with Drug-Susceptible TB

Option	Total Duration (Months)	Initial Phase		Continuation Phase[1]		Comments
		Drugs	Interval & Dose # (minimal duration)	Drugs	Interval & Dose # (minimal duration)	
1	6	Isoniazid Rifampin Pyrazinamide Ethambutol	Daily DOT for 40 doses (8 wks.)	**Regimen (1a) INH/RIF** **OR**	**DOT - 7 days/week for 126 doses (18 weeks)** **OR**	Regimen must be directly observed. Continue Ethambutol until susceptibility to Isoniazid and Rifampin is obtained via drug susceptibility results.
				Regimen (1b) INH/RIF **OR**	***DOT- 5 days/week for 90 doses (18 weeks)** **OR**	
				Regimen (1c) INH/RIF	**Thrice-weekly DOT for 54 doses (18 weeks) is preferred treatment**	
Pyridoxine (Vitamin B6) 25 - 50 mg PO daily to prevent the development of Isoniazid-induced peripheral neuropathy.						

INH=Isoniazid RIF=Rifampin PZA=Pyrazinamide EMB=Ethambutol Vitamin B6=Pyridoxine

NOTE:
a. ***Daily DOT = 5 days/week (Monday through Friday). Self-administered doses (including those on weekends) will not be counted toward the total doses. 5 daily doses of DOT equal 3 thrice-weekly doses of DOT. **Intermittent therapy is not recommended for HIV (+) individuals.**
b. Split dosing should be avoided.
c. Rifamate, a fixed combination of Rifampin 300 mg, and Isoniazid 150 mg, may be used to minimize the number of pills. Intermittent dosing is not recommended with fixed combination medications.
d. Refer to current drug reference or drug package insert for a complete list of adverse drug
e. reactions and drug interaction.

[1] TB treatment may be extended beyond 6 months minimal duration as determined by consultation with and documentation from delegating physician.

Table 2: First-Line TB Drugs Dosages

Drugs	Adult Dose based on body weight in kilograms (kg)[2]		Adverse Reactions
	Daily	**Thrice-Weekly (preferred over twice weekly)**	
Isoniazid	300 mg (5 mg/kg max. dose 300 mg) **No Less than 300mg/day**	900 mg (15 mg/kg max. dose 900 mg)	• Gastrointestinal (GI) upset • Liver enzyme elevation • Acute hepatitis • Peripheral neuropathy • Mild effects on central nervous system • Drug interactions
Rifampin	600 mg	600 mg	• Orange discoloration of body fluids and secretions • Drug interactions • GI upset • Hepatitis • Easy bruising/ bleeding • Influenza-like symptoms • Rash
Pyrazinamide[3]	40-55 kg: 1000 mg 56-75 kg: 1500 mg 76+ kg: 2000 mg	40-55 kg: 1500 mg 56-75 kg: 2500 mg 76+ kg: 3000 mg	• GI upset • Joint aches • Hepatitis • Rash • Hyperuricemia • Gout (rare)
Ethambutol	40-55 kg: 800 mg 56-75 kg: 1200 mg 76+ kg: 1600 mg	40-55 kg: 1200 mg 56-75 kg: 2000 mg 76+ kg: 2400 mg	• Optic neuritis

2 Formula used to convert pounds to kilograms: Divide pounds by 2.2 to get kilograms. *Example: Patient weighs 154 pounds ÷ 2.2 = 70 kilograms.*

3 Calculate Pyrazinamide and Ethambutol doses using actual body weight. NOTE: Round up fractions of a dose to the nearest whole number. Obese patients' (BMI over 30), underweight patients' (BMI under 17) and adults over 75 years dosing should be determined in collaboration with the district delegating/contract TB physician.

NOTE: Ethambutol and Pyrazinamide dosage adjustment may be needed if there is renal impairment. Patients with estimated creatinine clearance less than 70 mL/min or those with end-stage renal disease on dialysis are considered to be persons with complicated TB disease and dosing should be REFERRED to the district contract TB physician or delegating physician for care; a patient with these conditions cannot be managed using this protocol.

PATIENT EDUCATION/COUNSELING

(Reinforce pertinent information with handouts)

Education/communication should use methods adapted to patient's cultural and linguistic background. Provide education to the patient and his/her family, when family is available and document in the patient record.

1. The *"12 Points of Tuberculosis (TB) Patient Education"* and the *"Patient Tuberculosis Education Record"* is located on the TB web pages at http://dph.georgia.gov/sites/dph.georgia.gov/files/TB-ClinicForm12_Points_PtEd.pdf

    a. Transmission of Tuberculosis
    b. Differences between latent TB infection (LTBI) and active TB disease
    c. Progression of LTBI to active TB disease
    d. Signs and symptoms of TB disease
    e. **Importance of HIV testing and greater risk of progression to active TB if HIV infected**
    f. Respiratory isolation and use of masks
    g. Infectious period
    h. Importance of chemotherapy as prescribed
    i. Side effects and adverse medication reactions
    j. Directly observed therapy
    k. Importance of regular medical assessments
    l. Importance of contact identification

2. **For women on Rifamycin (Rifampin, Rifabutin, Rifapentine), review the importance of using an alternative or back-up method of birth control such as condoms, a copper-bearing IUD or diaphragm. Advise patients that Rifamycin use can reduce the effectiveness of combined oral contraceptives, progestin-only oral contraceptives, Levonorgestrel implants, Depo-Provera, the patch and ring**.

3. The patient's immunization status. Assess and refer or administer vaccines indicated according to the current Advisory Committee on Immunization Practices (ACIP) childhood and adult immunization schedule.

   For persons scheduled to receive a TST **or IGRA**, testing should be done either on the same day as vaccination with live-virus vaccine OR 4-6 weeks after the administration of the live-virus vaccine and at least one month after smallpox vaccination**.**

   See the Georgia Immunization Program Manual, Recommended Schedule and Guidelines, for current ACIP schedules and administration guidelines for each vaccine. The Georgia Immunization Manual may be accessed online at **http://dph.georgia.gov/immunization-section**

4. **Mental health assessment: If mental health problems are known, suspected, or patient answers "yes" to two or more related screening questions on F-3121R, send referral to the appropriate mental health agency or follow district policy.**

5. **Pre-diabetes education and counseling recommended for HgbA1C 5.7% or greater. Refer patient to Nutritionist, Primary Care Physician, or provide additional counseling which may be assessed online at http://dph.Georgia.gov/diabetes**

FOLLOW-UP

NOTE: Any hospital admissions or deaths of persons with TB disease are to be reported immediately **to the District TB Coordinator who will then report to the State TB Program.**

1. Continued patient management/follow-up by a case management team **comprising the patient**, PHN, physician and others determined by an individual needs assessment. Refer to the *TB Program Policy and Procedure Manual, **current edition*** and *Tuberculosis Nursing: A Comprehensive Guide to Patient Care, 2nd Edition* located in each county health department and *"*Scaled Goal Matrix Tool: Uniform Clinical Performance Measures for TB Nurse Case Managers, 2006" located on the TB web pages at **https://dph.georgia.gov/tb-public-health-clinic-forms**

2. After the nursing assessment, the PHN will use the *"Case*

Management Timeline – A Tracking Form for TB Medical Records" located on the TB web pages at **https://dph.georgia.gov/tb-public-health-clinic-forms** to determine documents to forward for review by the district TB coordinator, the district's contract physician and the state office.

3. Review the respiratory isolation status for the patient**.** All 3 of the following criteria must be met before isolation can be discontinued: patient has three consecutive negative AFB sputum smear results; patient has received standard anti-tuberculosis treatment for a minimum of two weeks; and patient has demonstrated clinical improvement.

   After the baseline 3 consecutive sputum specimens, collect follow-up sputum samples as follows:

   a. You may collect up to three sputum samples in a week until three consecutive negative AFB smears are obtained to determine when to discontinue respiratory isolation. Only one sputum sample that week should be marked on the lab form for smear/culture/sensitivity. Any additional sputum samples of the same week should be examined for AFB smear only.

   b. After three consecutively negative sputum smears are obtained, collect only one sputum specimen for smear/culture/sensitivity weekly until culture converts to negative.

   c. After sputum culture converts to negative, collect one sputum specimen monthly thereafter for smear/culture/sensitivity.

   d. Collect one sputum specimen at 60 days after medication treatment initiation for smear/culture/sensitivity test. A positive culture at this point identifies patients at increased risk for relapse. If the culture is still positive, refer patient for treatment to the contract physician.

   e. If the patient is unable to produce sputum **spontaneously, attempt to collect using nebulized sputum induction guidelines per procedure in the TB Policy & Procedure Manual, current version.** Document the collection attempt.

4. Monitor patient monthly for adverse drug reactions, drug-drug

interactions, drug-food interactions, drug-lab interactions, infectious status, and clinical and bacteriologic response to therapy.

5. Provide HIV test results with post-test counseling to patient and, if positive, appropriate referrals to HIV care. Seek confirmation that patient kept referral appointment for HIV care. If assistance is needed in linking patients to HIV care, please see the following website: https://www.gacapus.com/r/resource-directory-2/
   A Georgia Ryan White HIV Clinic list can also be found at https://dph.georgia.gov/care-services

6. Conduct contact identification following the *Tuberculosis Policy and Procedure Manual,* the *Tuberculosis Nursing: A Comprehensive Guide to Patient Care, 2nd Edition,* and the *CDC Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis* (current edition).

7. Perform the following blood chemistry tests monthly to monitor reactions to TB drugs:

   a. AST and ALT
   b. Bilirubin
   c. Alkaline phosphatase
   d. CBC with platelets
   e. Serum creatinine monthly only if there are abnormalities at baseline or there are clinical reasons to obtain the measurements (e.g., hepatitis B or C virus infection, alcohol abuse, and abnormal kidney function)

   NOTE: Discontinue Isoniazid and/or Rifampin and report immediately to the consulting physician if any of the following occur:

   1) AST/ALT levels equal to or greater than 3 times the upper limit of normal with symptoms of adverse reactions.
   2) AST/ALT levels equal to or greater than 5 times the upper limit of normal in an asymptomatic patient.
   3) Patient reporting symptoms of adverse reactions.

8. Monitor the vision of patients taking Ethambutol by providing vision checks monthly, including visual acuity and red/green color discrimination.

9. Adherence should methodically be assessed monthly, at a minimum.

10. Observe the patient for Isoniazid-induced peripheral neuropathy (e.g., tingling, numbness, pain) during therapy. If present, report to the delegating physician immediately**.**

11. If patient is a woman of child-bearing age, assess date of last menstrual period monthly. Perform pregnancy test as needed.

NOTE: Consult delegating physician when further medical guidance is needed and/or the TB nurse protocol is not applicable for therapeutic treatment of patient.

1. **For patients with the following conditions, REFERRAL to the delegating physician is required and patients cannot be treated under this protocol.**

   a. TB treatment for children **from birth up to 15 years of age (i.e., age 0 – 14 years)**
   b. Any known drug resistance to anti-TB medications
   c. Known HIV infection
   d. Central Nervous System (CNS) TB
   e. TB pericarditis
   f. TB patient requiring adjunctive use of corticosteroid therapy
   g. Use of once-weekly Isoniazid and Rifapentine in continuation phase for active TB disease
   h. Renal insufficiency with estimated creatinine clearance less than 70 ml/min
   i. End-stage renal disease on hemodialysis
   j. Any TB patient requiring 2nd line TB drugs
   k. Treatment failure (positive culture of *M. tb* after 4 months of treatment)
   l. Treatment of Suspected TB Meningitis

      NOTE: Consult delegating physician when further medical guidance is needed and/or the TB nursing protocol is not applicable for therapeutic treatment of patient.

2. Refer patient to a licensed dietitian if indicated. This will be especially important if the patient has a history of drug or alcohol abuse, is pregnant or breastfeeding, is HIV positive, has gastrointestinal side effects from TB drugs **or other medications,** has history of eating disorder or **if BMI is greater than 30 or less than 17.**

3. If patient needs housing, food or other frontline services, consult with the Georgia TB Program's Social Worker.

4. If smoker or tobacco user, refer to a local cessation program and/or the Georgia Tobacco Quit Line, 1-877-270-STOP (7867**).**

5. If substance abuse **is** known or suspected, refer for appropriate counseling**. If mental health problems are known or suspected, refer to appropriate agency for counseling and intervention.**

Table 3: TREATMENT OF TB - DRUG INTERACTIONS

Obtain and record a complete list of current prescription medications (including dose and frequency) from each LTBI and TB patient. Check for interactions between each of their medications and the planned LTBI/TB medications using a current drug reference. We recommend using Lexicomp, as all public health staff has access to this resource: https://online.lexi.com/lco/action/home;jsessionid=de081f2350de3dbc91e. The examples listed below are not exhaustive and do not substitute for the steps outlined above.

MEDICATION INTERACTIONS – RIFAMPIN and other Rifamycins (Rifapentine, Rifabutin)

Some Common Drugs/Drug Classes	**Effect on the co-administered drug**
Anticoagulants (Warfarin, Coumadin)	↓ serum concentration
Sulfonylureas (Glipizide, Glyburide, Glimepiride)	↓ serum concentration
Thiazolidinediones (Rosiglitazone, Pioglitazone)	↓ serum concentration
Contraceptives (oral, implants, patch, ring, injections)	↓ serum concentration
Fluconazole, Voriconazole, Itraconazole	↓ serum concentration
Corticosteroids	↓ serum concentration
Narcotics/analgesics (Methadone)	↓ serum concentration
Atovaquone (Mepron)	↓ serum concentration
Dapsone	↓ serum concentration
Cyclosporine	↓ serum concentration
Quinidine	↓ serum concentration
Lamotrigine (Lamictal)	↓ serum concentration
Phenytoin (Dilantin)	↓ serum concentration
Valproic acid and derivatives (Depakene, Depakote)	↓ serum concentration
Buspirone (Buspar)	↓ serum concentration
Thyroid hormone replacement	↓ serum concentration

DRUG INTERACTIONS – ISONIAZID

Name/type	**Effect on the co-administered drug**

Diazepam (Valium)	↓ serum concentration ↑ half-life
Phenytoin (Dilantin)	↑ serum concentration ↑ toxicity
Carbamazepine (Tegretol)	↑ serum concentration ↑ toxicity
Citalopram (Celexa)	↑ serum concentration ↑ toxicity
Alcohol	↑ risk of Isoniazid-**induced** hepatitis
Antacids	should be taken two hours apart, otherwise Isoniazid will have no effect

HIV: Antiretroviral therapy and TB medications

The information on interactions with Rifampin and HIV antiretroviral therapy (ART) is constantly changing; all people living with HIV (PLWH) should be referred to the contract physician for care. In general, only certain HIV medications can be used and Rifampin may be replaced by Rifabutin if appropriate to accommodate choice of ART. Rifabutin is on the formulary at the state pharmacy.

Recommended resource for HIV treatment guidelines and medication interactions: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/284/pi-drug-interactions

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STANDARD NURSE PROTOCOL FOR LATENT TUBERCULOSIS INFECTION (LTBI) AND PRESUMPTIVE LTBI

DEFINITION

LTBI means that a person has been infected with M.tuberculosis (M.tb) but has no clinical or radiographic evidence of active TB disease. Individuals who are infected but do not have active disease are not infectious but, if not adequately treated, are at risk for developing disease and becoming infectious in the future.

Presumptive LTBI treatment is the practice of providing window period prophylaxis treatment to high-risk persons exposed to infectious people with TB disease. This means, when these exposed persons have an initial negative tuberculin skin test (TST) reaction (less than 5mm induration) or negative interferon gamma release assay (IGRA) test result and the test was performed less than eight weeks from the person's last exposure to a person with TB disease, treatment for LTBI is started until a follow-up TST/IGRA is negative. The window period is the time span between the date of a negative initial TST or IGRA and the date of the follow-up TST or IGRA.

Exposed persons at particularly high-risk of developing TB disease once infected with *M.tb* include: children less than 5 years of age and persons with compromised immune systems; compromised by HIV infection, medications (Prednisone, cancer chemotherapy, anti-rejection drugs for cancer therapy, tumor necrosis factor alpha agents antagonists) and certain medical conditions (diabetes mellitus, silicosis, end stage renal disease, cancer of the head and neck, reticuloendothelial diseases [e.g., lymphoma, leukemia], gastric or jejunoileal bypass surgery). These persons would benefit from presumptive LTBI therapy.

ETIOLOGY

Causative agent of TB is the *Mycobacterium tuberculosis* (*M.tb*) complex (*M. tuberculosis, M. bovis, M. africanum, M. microti, M. canetii, M. caprae, M.mungi and M. pinnipedii)*.

SUBJECTIVE

1. Patient may have a history of known exposure to a person with TB.

2. Patient has no symptoms of TB disease.

NOTE: A complete medical history and review of current medications is required to determine if there are any diseases/illnesses present that would require consultation or referral to delegating physician.

OBJECTIVE

1. Physical examination performed per programmatic guidelines shows

no signs of active TB disease present.

NOTE: If signs and symptoms of TB disease are evident, patient should have 3 consecutive negative sputum smears and negative cultures with evaluation by a clinician**/**delegating physician before starting treatment for LTBI.

ASSESSMENT

1. Latent tuberculosis infection

2. Presumptive latent tuberculosis infection during the window period

PLAN

The desired outcome of treatment is to decrease high-risk persons' chance of developing active TB disease once diagnosed with latent TB infection.

NOTE: Any hospital admissions or deaths of persons with TB disease are to be reported immediately **to the District TB Coordinator who will then report to the State TB Program.**

DIAGNOSTIC STUDIES

1. If positive results for either an IGRA or a TST cannot be verified (including millimeters [mm] of induration), perform a TST or IGRA. **An IGRA is the preferred method of testing in individuals greater than or equal to 2 years of age who are foreign born and/or have a history of BCG vaccination. TB skin testing should be performed on children less than 2 years of age.** Vaccination with live viruses may interfere with either of these test reactions. For persons scheduled to receive a TST **or IGRA, testing should be done as follows:**

    a. Either on the same day as vaccination with live-virus vaccine

    OR

    b. 4-6 weeks after the administration of the live-virus vaccine. At least one month after smallpox vaccination.

2. Perform the following baseline blood chemistry labs:

    a. Obtain aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, **Hemoglobin A1C**, and Hepatitis C antibody for all adults.

Normal (HgbA1C)	**Below 5.6%**
Pre-Diabetes (HgbA1C)	**5.7% - 6.4%**
Diabetes (HgbA1C)	**6.5% or greater**

Note: If Hemoglobin A1C (HgbA1C) is elevated, between 5.6% - 6.4%, refer to nutritionist or primary care physician for prediabetes education and counseling and if equal or greater than 6.5%, refer patient to primary care physician for evaluation and follow up.

Note: If Hepatitis C Ab is positive, refer patient to primary care physician for evaluation and follow up.

b. Hepatitis B profile **(HBsAg, HBsAb, HBsAb)** should be obtained for all adults (regardless of birth country) and anyone less than 18 years old who is foreign-born.

Note: If **HBsAg** is positive, refer to primary care physician for evaluation and consideration for treatment. **If all Hepatitis B serology results are negative (i.e., the patient is susceptible to Hepatitis B infection), consider Hepatitis B immunization as per ACIP guidelines.**

3. All individuals 13 years and older will be tested for HIV using the opt-out approach. Consent is inferred unless patient declines testing. Individuals younger than 13 years old should also be tested for HIV using the opt-out approach if the individual is sexually active or abuses drugs. If HIV positive, collaborate with HIV Program to obtain CD4 T-cell count, then refer to consulting physician.

4. **Urine pregnancy test, if woman is of childbearing age and sexually active.**

5. Baseline complete blood count with platelets for patients on the Isoniazid-Rifapentine regimen and Rifampin regimen.

6. Chest x-ray performed to detect abnormalities compatible with TB disease. (Radiographic findings of healed, inactive TB and reactivating TB sometimes cannot be distinguished).

7. If any lab results are abnormal, consult with delegating physician.

NOTE: **With the exception of HIV testing**, the baseline lab measurements are not mandatory for children less than **15 years** of age, unless a complicating medical condition (e.g., HIV, liver disease, renal disease, cardiac disease), foreign born requiring Hepatitis B testing or high-risk lifestyle is known or suspected.

LABORATORY FINDINGS

1. Chest x-ray negative for evidence of tuberculosis disease.

2. Absence of clinical signs of TB disease, both pulmonary and extra-pulmonary.

3. Patients with the following conditions/illnesses should be treated for LTBI if they have a positive TST **(5 mm or greater)** and/or positive IGRA:

    a. HIV-positive
    b. Recently exposed to a person with TB disease
    c. Fibrotic changes on chest x-ray consistent with old TB
    d. Organ transplants recipients
    e. Candidates being considered for treatment with tumor necrosis factor (TNF) antagonists such as injectable Remicade [Infliximab] for rheumatologic conditions or ulcerative colitis prior to initiation of therapy)
    f. Persons receiving the equivalent of equal to or greater than 15mg daily of prednisone for 1 month or longer

4. Patients with the following conditions/illnesses should be treated for LTBI if they have a positive TST **(10 mm or greater)** and/or positive IGRA:

    a. People who have lived or spent time in high prevalence countries.
    b. Injection drug users.
    c. Residents and employees of high-risk congregate settings (e.g., correctional facilities, nursing homes and other long-term care facilities, homeless shelters, hospitals and other health care facilities).
    d. Mycobacteriology laboratory personnel.
    e. Persons with clinical conditions that place them at high risk of progression to TB disease (e.g., substance abuse, infection with *M.tb* within the past two years, diabetes, hematologic or

reticuloendothelial malignancies, chronic renal failure, post-gastrectomy, silicosis, immunosuppressive therapy, chronic malabsorption syndromes)

f. Children less than 5 years of age, or children and adolescents exposed to adults in high-risk groups.

5. Patients with no risk factors should be treated for LTBI if they have a positive TST (**15mm or greater**) and/or positive IGRA.

6. Persons exposed to a person with TB disease may be treated for presumptive LTBI. Exposed persons with suppressed immune systems due to HIV infection, prolonged corticosteroid therapy, organ transplant and/or use of tumor necrosis factor alpha inhibitors should be treated for presumptive LTBI with a full course of LTBI treatment, regardless if follow-up TST/IGRA is negative.

7. There is also a group of people that can be treated for presumptive LTBI but do not have to complete a full course of LTBI treatment (as discussed above). The following exposed persons being treated for presumptive LTBI treatment can stop treatment if the follow-up TST/IGRA is negative:

    a. Child less than 5 years of age.
    b. Person diagnosed with diabetes mellitus, silicosis, end stage renal disease, gastrectomy, jejunoileal bypass, leukemia, lymphoma, and/or cancer of the head or neck.

NOTE: Treatment of LTBI or presumptive LTBI might NOT be indicated for persons likely to be infected with drug-resistant *M.tb*. These persons should be referred to the delegating physician.

NOTE: Treatment of LTBI might NOT be completed on persons who have been exposed to a person later found not to have TB. The Public Health Nurse (PHN) should consult with the delegating physician for care.

THERAPEUTIC

PHARMACOLOGIC

NOTE: Order medications for treatment from drug stock and send a copy of the drug order(s) to the District Pharmacist or District Drug Coordinator. Refer to Tables 1 and 2 for options and dosages.

1. If a patient is referred to the delegating physician, the PHN may not dispense ANY of the prescribed medications**.** A pharmacist or dispensing ***practitioner*** can dispense the TB medications, or the prescription may be called in **or E-scribed** to a pharmacy by the **prescribing** physician.

2. PHN may dispense Rifapentine when given in conjunction with Isoniazid for LTBI treatment. PHN may not dispense 2nd line TB medications. If 2nd line medications are ordered, a pharmacist or dispensing practitioner can dispense the 2nd line TB medications, or the prescription may be called in **or E-scribed** to a pharmacy by the **prescribing** physician.

VIDEO DIRECTLY OBSERVED THERAPY (VDOT)

Carefully selected patients meeting established minimum criteria may be eligible to receive their medications via VDOT. In order to perform VDOT the healthcare worker observes the patient take their medication via smartphone, laptop, or desktop. See Tuberculosis Policy and Procedure Manual for additional information.

PATIENT EDUCATION/COUNSELING

(Reinforce pertinent information with handouts).

Education/communication should use methods adapted to patient's cultural and linguistic background. Provide education to the patient and his/her family, when family is available, and document in the patient record.

1. The *"12 Points of Tuberculosis (TB) Patient Education"* and the *"Patient Tuberculosis Education Record"* is located on the TB web pages at http://dph.georgia.gov/sites/dph.georgia.gov/files/TB-

ClinicForm12_Points_PtEd.pdf

a. Transmission of Tuberculosis
b. Differences between latent TB infection (LTBI) and active TB disease
c. Progression of LTBI to active TB disease
d. Signs and symptoms of TB disease
e. Importance of HIV testing and greater risk of progression to active TB if HIV infected
f. Importance of chemotherapy as prescribed
g. Side effects and adverse medication reactions
h. Directly observed therapy (if necessary)
i. Importance of regular medical assessments

2. **For women on Rifamycin (Rifampin, Rifabutin, Rifapentine), review the importance of using an alternative or back-up method of birth control such as condoms, a copper-bearing IUD or diaphragm. Advise patients that Rifamycin use can reduce the effectiveness of combined oral contraceptives, progestin-only oral contraceptives, Levonorgestrel implants, Depo-Provera, the patch and ring**.

3. The patient's immunization status. Assess and refer or administer vaccines indicated **per** the current Advisory Committee on Immunization Practices (ACIP) childhood and adult immunization schedule.

   For persons scheduled to receive a TST, testing should be done either on the same day as vaccination with live-virus vaccine **OR** 4-6 weeks after the administration of the live-virus vaccine and at least one month after smallpox vaccination.

   See the Georgia Immunization Program Manual, Recommended Schedule and Guidelines, for current ACIP schedules and administration guidelines for each vaccine. The Georgia Immunization Manual may be accessed online at http://dph.georgia.gov/immunization-section

FOLLOW-UP

NOTE: Children (under the age of 14 years) are not required to have routine follow-up labs regardless of treatment regimen.

1. At eight to ten weeks after initial TST/IGRA, a follow-up TST/IGRA is to be performed on exposed persons on window period prophylaxis. If the follow-up TST/IGRA is positive, treatment is to continue until a full course of LTBI treatment is completed.

   If the follow-up TST/IGRA is negative in an exposed person who is immunosuppressed, (due to HIV infection, prolonged corticosteroid therapy, organ transplant and/or use of tumor necrosis factor alpha inhibitors) a full course of LTBI treatment is required.

   If the follow-up TST/IGRA is negative in any other exposed person, then the window period treatment may be discontinued.

2. Monitor patients receiving LTBI therapy at least monthly for adverse drug reactions (such as hepatitis, peripheral neuropathy), drug-drug interactions, drug-food interactions, drug-lab interactions, adherence**.**

   NOTE: Any hospital admissions or deaths of persons with TB disease are to be reported immediately **to District TB Coordinator who will then report to the State TB Program.**

   a. Observe the patient for Isoniazid-induced peripheral neuropathy (e.g., tingling, numbness, pain) during therapy. If present, refer to the delegating physician immediately**.**

   b. Symptoms of hepatitis (nausea, loss of appetite, vomiting, persistently dark urine, yellowish skin, malaise, unexplained elevated temperature for more than three days, abdominal tenderness and/or right upper quadrant tenderness). If present, put all LTBI medications on hold, obtain AST/ALT levels and refer to the delegating physician immediately.

3. Provide HIV test results with post-test counseling to patient and, if positive, appropriate referrals to HIV care. Seek confirmation that patient kept referral appointment for HIV care. See the following website: https://www.gacapus.com/r/resource-directory-2/
   A Georgia Ryan White HIV Clinic list can also be found at

https://dph.georgia.gov/care-services

4. Obtain monthly AST/ALT for patients considered at risk of developing hepatotoxicity. These patients include those with:

    a. baseline liver test abnormalities
    b. Continued regular alcohol use
    c. Known liver disorders
    d. Postpartum[4] women

5. Hold all TB medications and refer to the delegating physician immediately if:

    a. AST/ALT levels equal to or greater than 3 times the upper limit of normal with symptoms of adverse reactions.
    b. AST/ALT levels equal to or greater than 5 times the upper limit of normal in an asymptomatic patient.
    c. Patient reporting symptoms of adverse reactions.

    NOTE: Any hospital admissions or deaths due to adverse reactions are to be reported immediately **to the District TB Coordinator who will report to the State TB Program.**

6. **Obtain monthly complete blood count (with platelets) for patients receiving the Isoniazid-Rifapentine or Rifampin regimen. Hold all TB medications and refer to delegating physician if any results are abnormal.**

7. If patient is a woman of child-bearing age, assess date of last menstrual period monthly. Perform pregnancy test as needed. If pregnancy test ever positive, hold all TB medications and refer to delegating physician immediately.

8. A clinical symptom screen is required for all patients who have a lapse in treatment. A repeat chest x-ray/evaluation is required for patients who are symptomatic or who have had a lapse in LTBI therapy for two months or more.

4 Period of time immediately after the birth of an infant through 6 weeks. Pregnant women, particularly African-American and Hispanic women, may be at increased risk for fatal hepatitis associated with Isoniazid, per some reports. This risk may be increased during the postpartum period. These patients should be closely monitored for adverse reactions throughout the course of treatment. The risk of hepatitis from Isoniazid in pregnant/postpartum women does NOT preclude treatment of LTBI if these women are at extremely high risk for developing active TB (e.g., in close contact of person with TB disease, HIV positive, or with documented recent infection or conversion).

9. **Identify those patients who are eligible for VDOT per the VDOT policy in the current edition of the TB Policy & Procedure Manual, current version.**

CONSULTATION/REFERRAL

1. For patients with the following conditions, CONSULTATION with the delegating physician is required for patients to be treated under this protocol. Consultation must be documented in the patient's record.

    a. Diabetes mellitus
    b. Liver disease
    c. Allergic reactions not requiring 2nd line TB drugs
    d. Review of current medications reveal potential for drug-drug interactions with TB medications.
    e. Treatment interruptions of two months or more
    f. HIV positive or refuses HIV testing
    g. Any abnormal lab results

    NOTE: Consult delegating physician when further medical guidance is needed and/or the LTBI nursing protocol is not applicable for therapeutic treatment of patient.

2. For patients with the following conditions, REFERRAL to the delegating physician is required. These patients would no longer be able to be treated under this protocol.

    a. Pregnant, breastfeeding or postpartum women
    b. Patients experiencing adverse reactions
    c. Patients with known exposure to a person with drug resistant TB disease
    d. Children age **2 years and older** who are close contacts for whom the Isoniazid and Rifapentine regimen may be considered because it offers practical advantages or because the child is unlikely to complete 9 months of daily Isoniazid.

    NOTE: Consult delegating physician when further medical guidance is needed and LTBI nursing protocol is not applicable for therapeutic treatment of patient.

3. If smoker or tobacco user, refer to a local cessation program and/or the Georgia Tobacco Quit Line, 1-877-270-STOP (7867).

4. If **mental health** or substance abuse is known or suspected, refer for appropriate counseling for **intervention and follow up**.

5. If patient needs housing, food or other frontline services, consult with the Georgia TB Program's Social Worker

TABLE A: LTBI MEDICATIONS IN PREFERRED PRIORITY RANKINGS

Priority rank*	Regimen	Recommendation Grade**
Preferred	3 months isoniazid plus Rifapentine given once weekly	Strong
Preferred	4 months Rifampin given daily	Strong
Preferred	3 months Isoniazid plus Rifampin given daily	Conditional
		Conditional
Alternative	6 months Isoniazid given daily	Strong[§]
		Conditional
Alternative	9 months Isoniazid given daily	Conditional

Modified from Table 3 in "Guidelines for the Treatment of LTBI: Recommendations of the NTCA and CDC, 2020. MMWR Recomm Rep 2020; 69(no, RR-1).

Abbreviation: HIV = human immunodeficiency virus

* *Preferred:* excellent tolerability and efficacy, shorter treatment duration, higher completion rates than longer regimens and therefore higher effectiveness; *alternative:* excellent efficacy but concerns regarding longer treatment duration, lower completion rates, and therefore lower effectiveness.

** ***Strong***: strong GRADE recommendation for a regimen was made if the panel concluded that the desirable consequences of the intervention outweighed the undesirable consequences, the **majority of well-informed patients would choose the regimen**, and the evidence was at least moderate quality; ***conditional****:* conditional GRADE recommendation was made for a regimen when uncertainty existed regarding whether the desirable consequences outweighed the undesirable consequences (e.g., low-quality evidence for a critical outcome such that additional evidence could change key findings, hence the recommendation). A conditional recommendation indicates that **well-informed patients might make different choices regarding whether to choose the regimen**.

[§] Strong recommendation for those persons unable to take a preferred regimen (e.g., due to drug intolerability or drug-drug interactions).

Table B: Treatment of LTBI – Recommended Drug Regimens [and Dosages for Adults and Children] (Select ONE Option)

Drug	Interval and Duration	Adult Dosage	Criteria for Completion	Comments
Option A **Isoniazid and Rifapentine**	**Once weekly for 12 doses**.	**Isoniazid**:15mg/kg PO (round up to the nearest 50 or 100 mg); 900mg PO max **Rifapentin**: 10-14kg 300mg PO; 14.1-25kg 450mg PO; 25.1-32kg 600mg PO; 32.1-49.9kg 750mg PO; Equal to or **greater than** 50kg 900mg (max dose) PO	11 doses within 16 weeks (doses may be given no more frequently than every 72 hours) **In ages 2-5 years old, all 12 doses may be given by DOT.** **In ages 5 years and older, all 12 doses may be given by DOT or self-administered therapy.**	**Isoniazid and Rifapentine is recommended and the preferred regimen for treating LTBI in otherwise healthy patients aged 2 years and older at high risk for developing active TB.** These patients include persons in close contact with person with TB disease, recent converters, HIV positive persons (NOT on antiretrovirals) and those with old, healed TB on chest x-ray. Isoniazid and Rifapentine **should** also be used in situations where it offers practical advantages **over other preferred regimens. Isoniazid and Rifapentine is NOT recommended for the following patients: children less than 2 years of age, pregnant women or women expecting to become pregnant during treatment, patients who have LTBI with presumed Isoniazid or Rifampin resistance, and persons taking medications with clinically significant or unknown drug interactions with rifapentine**. Refer to the contract physician children **aged 2 and older who are close contacts** for whom the Isoniazid and Rifapentine regimen **should** be considered because it offers practical advantages.
Option B **Rifampin**	Daily self-admin (7 days/ week) for 4 months (18 weeks) **OR** Daily DOT **(Mon-Fri)** for 4 months (18 weeks)	600mg PO **for all adults** (10 mg/kg **for children** - max dose 600mg) **OR** 600mg PO for **all adults** (10 mg/kg **for children** - max dose 600mg)	120 doses within 6 months **OR** 90 doses within 6 months	**Daily Rifampin is a preferred regimen for treatment of LTBI with a strong recommendation. Rifampin therapy is the only preferred regimen for persons who acquired LTBI from a TB patient with Isoniazid-resistant**, Rifampin susceptible TB disease**; Rifampin is not recommended for persons who are: Taking medications with clinically significant or unknown drug interactions with rifampin, presumed infected with Rif-resistant M.TB, and women who are pregnant or expect to become pregnant within the 4 month regimen.**

Option C **Isoniazid and Rifampin**	**Daily self-admin (7 days/week for 3 months (18 weeks)**	**Isoniazid: 300mg PO for all adults (5mg/kg) –** max dose 300mg **For children 300mg PO (5mg/kg) –** max dose 300mg **Rifampin: 600mg PO for all adults (10mg/kg)-** max dose 600mg **10mg/kg for children –** max dose 600mg	**90 doses within 6 months**	**A regimen of 3 months of daily Isoniazid plus Rifampin is a preferred treatment that is conditionally recommended for adults of all ages, children and for HIV –positive persons as drug interactions allow. Among children aged < 15 years specifically, a 3-month course of daily Isoniazid plus Rifampin appeared as effective as a 6 month or longer course of Isoniazid. Isoniazid and Rifampin is not recommended for the following adults: Persons taking medications with clinically significant or unknown drug interactions with rifampin, presumed infected with RIF-resistant M.TB, and women who are pregnant or expect to become pregnant within the 3 month regimen. Refer to the contract physician children aged 2 and older who are close contacts for whom the Isoniazid and Rifampin regimen may be considered because it offers practical advantages over the other preferred regimens.**
Option D **Isoniazid 6 Months** **OR**	**Daily self-admin (7 days/week) for 6 months** **OR** **Twice-weekly DOT for 6 months**	**300mg PO (5mg/kg – max dose 300mg)** **OR** **900mg PO (15mg/kg- max dose 900mg**	**180 doses within 9 months** **OR** **52 doses within 9 months**	**Isoniazid therapy for 6 months is strongly recommended as an alternative for those unable to take a shorter preferred regimen, e.g., due to drug-drug intolerability or drug-drug interactions particularly in HIV negative persons. In HIV positive patients, Isoniazid may be concurrently taken with nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors or non-nucleoside reverse transcriptase inhibitors (NNRTIs).** **NOTE: Twice weekly regimen not recommended for HIV positive patients.** **LTBI patients (including HIV infected) on daily INH LTBI regimen will no longer require DOT.** **Consider adding pyridoxine (Vitamin B6) 25-50mg to be given with each dose of isoniazid as a preventive measure against Isoniazid –induced peripheral neuropathy.**
Option D **Isoniazid 9 Months**	Daily self-admin (7 days/ week) for 9 months **OR** **Twice-weekly* DOT for 9 months**	300mg PO (5 mg/kg - max dose 300mg) **OR** **900mg PO (15 mg/kg - max dose 900mg)**	270 doses within 12 months **OR** **76 doses within 12 months**	In HIV-positive patients, Isoniazid may be taken concurrently with nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors, or non-nucleoside reverse transcriptase inhibitors (NNRTIs). **NOTE: Twice-weekly regimen not recommended for HIV positive patients. LTBI patients (including HIV-infected) on daily INH LTBI regimen will no longer require DOT.** Consider adding pyridoxine (Vitamin B6) 25 – 50 mg to be given with each dose of isoniazid as a preventive measure against Isoniazid-induced peripheral neuropathy.

*Twice-weekly doses should optimally be given at least two days apart, unless given to "catch up" on a missed dose. A dose given two consecutive days is discouraged. **NOTE:** Isoniazid is available in 100 and 300 mg tablets (both are scored for dividing in half (½). Rifapentine is available in 150 mg tablets only. **Rifampin (rifampicin) is available as 150-mg and 300-mg capsules. Rifampin and Rifapentine cannot be substituted for each other. NOTE**: DOT is **RECOMMENDED for all patients less than 5 years of age and patients on ANY biweekly INH (which is usually prescribed for children). The INH/Rifapentine regimen may be self administered or DOT – this is up to the discretion of the TB nurse.**

Table C: Treatment of LTBI – Drug Adverse Reactions and Monitoring

NOTE: The baseline lab measurements are not mandatory for children less than 15 years of age, unless a complicating medical condition (e.g., HIV, liver disease, renal disease, cardiac disease), foreign born requiring Hepatitis B testing or high-risk lifestyle is known or suspected.

Drug	Adverse Reactions	Monitoring **NOTE:** If any lab results abnormal, report to delegating physician.	Comments
Isoniazid	Gastrointestinal (GI) upset, hepatic enzyme elevations, hepatitis, peripheral neuropathy, mild effects on central nervous system, drug interactions	Obtain aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, **HgbA1C**, and Hepatitis C antibody for all adults. Hepatitis B profile should be obtained for all adults (regardless of birth country) and anyone less than 18 years old who is foreign-born. All individuals will be tested for HIV using the opt-out approach. Consent is inferred unless patient declines testing. If HIV positive, collaborate with HIV Program to obtain CD4 T-cell count. Consult with delegating physician. See **CONSULTATION on P.733** Baseline complete blood count with platelets for patients on the Isoniazid-Rifapentine regimen or Rifampin regimen**.**	Hepatitis risk increases with age and alcohol consumption, **but these are not contraindications to prescribing INH.** Pyridoxine can prevent isoniazid-induced peripheral neuropathy.
Rifampin and Rifapentine	Orange discoloration of body fluids (secretions, tears, urine), GI upset, drug interactions, hepatitis, thrombocytopenia, rash, fever, Influenza-like symptoms, hypersensitivity reaction[5]	Obtain aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, **HgbA1C**, and Hepatitis C antibody for all adults**.** Hepatitis B profile should be obtained for all adults (regardless of birth country) and anyone less than 18 years old who is foreign-born. All individuals will be tested for HIV using the opt-out approach. Consent is inferred unless patient declines testing. If HIV positive, collaborate with HIV Program to obtain CD4 T-cell count. Consult with delegating physician. See **CONSULTATION on p.733** Baseline complete blood count with platelets for patients on the Isoniazid-Rifapentine regimen or Rifampin regimen**.**	Hepatitis risk increases with age and alcohol consumption, **but these are not contraindications to prescribing Rifamycins.**

[5] Hypersensitivity reactions may include a flu like syndrome (e.g. fever, chills, headaches, dizziness, and musculoskeletal pain), thrombocytopenia, shortness of breath or other signs and symptoms including wheezing, acute bronchospasm, urticaria, petechiae, purpura, pruritus, conjunctivitis, angioedema, hypotension or shock. If moderate to severe reaction (e.g., thrombocytopenia, hypotension), hospitalization or life-threatening event: discontinue treatment. If mild reaction (e.g., rash, dizziness, fever): Continue to monitor patient closely with a low threshold for discontinuing treatment

Table D: Treatment of LTBI – Drug Interactions

NOTE: Obtain and record a complete list of current prescription medications (including dose and frequency) from each LTBI and TB patient. Check for interactions between each of their medications and the planned LTBI/TB medications using a current drug reference. We recommend using Lexicomp, as all public health staff has access to this resource: https://online.lexi.com/lco/action/home;jsessionid=de081f2350de3dbc91e. The examples listed below are not exhaustive and do not substitute for the steps outlined above.

MEDICATION INTERACTIONS – RIFAMPIN

Name/type	**Effect**
Anticoagulants (Warfarin, Coumadin)	↓ serum concentration
Sulfonylureas (Glipizide, Glyburide, Glimepiride)	↓ serum concentration
Thiazolidinediones (Rosiglitazone, Pioglitazone)	↓ serum concentration
Contraceptives (oral, implants, patch, ring, injections)	↓ serum concentration
Fluconazole, Voriconazole, Itraconazole	↓ serum concentration
Corticosteroids	↓ serum concentration
Narcotics/analgesics (Methadone)	↓ serum concentration
Atovaquone (Mepron)	↓ serum concentration
Dapsone	↓ serum concentration
Cyclosporine	↓ serum concentration
Quinidine	↓ serum concentration
Lamotrigine (Lamictal)	↓ serum concentration
Phenytoin (Dilantin)	↓ serum concentration
Valproic acid and derivatives (Depakene, Depakote)	↓ serum concentration
Buspirone (Buspar)	↓ serum concentration
Thyroid hormone replacement	↓ serum concentration

DRUG INTERACTIONS – ISONIAZID

Name/type	**Effect**
Diazepam (Valium)	↓ serum concentration ↑ half-life
Phenytoin (Dilantin)	↑ serum concentration ↑ toxicity
Carbamazepine (Tegretol)	↑ serum concentration ↑ toxicity
Citalopram (Celexa)	↑ serum concentration ↑ toxicity
Alcohol	↑ risk of Isoniazid-**induced** hepatitis
Antacids (Should be taken two hours apart, or Isoniazid will have no effect)	
Cycloserine	↑ risk of CNS toxicity

HIV: Antiretroviral therapy and medications for LTBI

The information on interactions with Rifamycins and HIV antiretroviral therapy (ART) is constantly changing; all people living with HIV (PLWH) should be referred to the contract Physician for care. In general, only certain HIV medications can be used in combination with Rifamycins.

Recommended resource for HIV treatment guidelines and medication interactions: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/284/pi-drug-interactions

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