
**STANDARD
NURSE PROTOCOLS
FOR
TUBERCULOSIS (TB)**

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TABLE OF CONTENTS

TUBERCULOSIS	6
Uncomplicated Pulmonary TB (Age 16 And Over)	6.1
Table 1: Regimen Options - Treatment of Clients With Drug-Susceptible TB	6.5
Table 2: First-Line TB Drugs	6.6
Table 3: Treatment of TB - Drug Interactions	6.13
Table 4: Drug Interactions - Rifampin	6.14
Table 5: Drug Interactions - Isoniazid	6.16
Latent TB Infection (LTBI)	6.19
Table A: Treatment of LTBI – Recommended Drug Regimens For Adults	6.27
Table B: Treatment of LTBI – Recommended Drug Regimens For Children	6.28
Table C: Treatment of LTBI – Drug Adverse Reactions And Monitoring	6.29
Table D: Treatment of LTBI – Drug Interactions (Format 1)	6.30
Table E: Treatment of LTBI – Drug Interactions (Format 2)	6.31
Table F: Drug Interactions – Isoniazid	6.33
Table G: Pediatric Dosages – Isoniazid In Children and Adolescents	6.34
Table H: Pediatric Dosages – Rifampin in Children and Adolescents	6.35
Table I: Isoniazid and Rifapentine Dose Amounts for Clients	6.36

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**STANDARD NURSE PROTOCOL FOR
UNCOMPLICATED PULMONARY TUBERCULOSIS (TB)
(AGE 16 AND OVER: Treatment for children from birth through 15 years requires
referral to district contract TB physician)**

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 (NAA) test for *Mycobacterium tuberculosis* is necessary to confirm the diagnosis of a tuberculosis case. However, suspected cases may be diagnosed on the basis of: a positive sputum 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. canettii*, *M. caprae*, *M.mungi* and *M. pinnipedii*).

SUBJECTIVE If any of the following conditions are present, the case is considered a complicated TB case and TB treatment must be ordered by the district contract TB physician:

1. Children from birth through 15 years
2. Extrapulmonary TB
3. Currently pregnant or breast-feeding
4. Known history of infection or exposure to multiple drug resistant (MDR) *M. tuberculosis*, or any drug resistance on susceptibility testing
5. Known HIV infection
6. Other new and/or complicated acute or chronic medical conditions including (but not limited to): diabetes, renal insufficiency with estimated creatinine clearance less than 50 ml/min., end-stage renal disease on hemodialysis
7. BMI greater than 30
8. Known allergies to anti-tuberculosis drugs
9. Treatment with once-weekly isoniazid and rifapentine during the continuation phase
10. Decision to extend the continuation phase longer than four months.

a. Sputum culture collected 60 days (2 months) after treatment initiation is positive

Individuals with **uncomplicated pulmonary TB**:

1. May have history of exposure to a known case
2. May have one or more of the following:
 - 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. Easy fatigability
 - g. Loss of appetite
 - h. Weight loss without dieting
 - i. Hemoptysis (coughing up blood)

OBJECTIVE

1. The following criteria are **useful in identifying** a suspected **pulmonary TB** case:
 - a. A **positive interferon gamma release assay (IGRA)** or a positive Mantoux tuberculin skin test. (The absence of a **positive IGRA** or reaction to the skin test does not rule out the diagnosis of TB disease or latent TB infection).
 - b. Positive staining of acid-fast bacillus (AFB) in sputum(s), bronchial brush, wash or lung tissue biopsy. (However, cases can be smear negative).
 - c. Chest x-ray showing abnormalities compatible with TB **disease. (Radiographic findings of healed, inactive TB and reactivating TB sometimes cannot be distinguished).**
 - d. **Symptoms compatible with TB (See Subjective: #2, p. 6.1) which** respond to treatment with anti-tuberculosis drugs.
2. **The following criteria (one or more) are required for a confirmed diagnosis of pulmonary TB:**
 - a. **Pulmonary** pathology findings compatible with the diagnosis of TB.

- b. **Respiratory specimens with positive culture or positive Nucleic Acid Amplification (NAA) test for *Mycobacterium tuberculosis*.**

ASSESSMENT

- 1. Uncomplicated pulmonary tuberculosis

OR

- 2. **Suspected case of uncomplicated** pulmonary tuberculosis

PLAN

DIAGNOSTIC STUDIES

- 1. **If positive interferon gamma release assay (IGRA) or a tuberculin skin test results cannot be verified (including millimeters [mm] of induration), perform a Mantoux tuberculin skin test or interferon gamma release assay (IGRA). Vaccination with live viruses may interfere with tuberculin skin test reactions. For persons scheduled to receive a tuberculin skin test, testing should be done as follows: Either on the same day as vaccination with live-virus vaccine or 4-6 weeks after the administration of the live-virus vaccine. At least one month after smallpox vaccination.**
- 2. Collect 3 sputum specimens (on consecutive days) for AFB smear/culture (and sensitivities on first sputum) and send to the **Georgia Public Health** Laboratory in Decatur. The public health nurse (PHN) will obtain the first sputum specimen and provide the client with two additional containers for collection and mailing of the next two consecutive early morning sputum specimens to the state laboratory. Instruction should be given to both client and family on how to properly produce sputum for examination. Seek client confirmation regarding mailing of specimens and check with the laboratory to confirm receipt of specimens. If necessary, the PHN should collect and mail the specimens.
- 3. Collect blood to obtain baseline measurements for the following lab tests:
 - a. Obtain aspartate aminotransferase (AST) [formerly, serum glutamic oxaloacetic transaminase (SGOT)], alanine aminotransferase (ALT) [formerly, serum glutamic-pyruvic transaminase (SGPT)], bilirubin, alkaline phosphatase, CBC with platelet count, serum uric acid, serum creatinine, **glucose, and Hepatitis C antibody** for all adults. **If glucose is above normal range (per reported parameters), obtain a hemoglobin A1C at next visit. On**

- known diabetics, obtain a hemoglobin A1C with baseline lab tests.**
- b. **Hepatitis B profile should be obtained for all adults (regardless of birth country) and anyone less than 18 years old who is foreign-born.**
 - c. All individuals will be tested for HIV using the opt-out approach. Consent is inferred unless client declines testing. If HIV-infected, collaborate with HIV Program to obtain CD4 T-cell count, then refer to consulting physician. (See REFERRAL section on pp. **6.12**).
4. Obtain baseline visual acuity testing and red/green color discrimination for clients being placed on ethambutol.
 5. Pregnancy test, if indicated.
 6. Baseline weight. (Compare client's baseline weight to usual weight for increase or decrease).
 7. **Record height. Calculate current BMI and record under initial weight. The following website provides a tool for calculating BMI: <http://www.cdc.gov/healthyweight/assessing/bmi/>**

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.

1. Order DOT for all doses until completion of treatment (see Tables 1 and 2 on pages **6.5** and **6.6** for options and dosages).
2. Pyridoxine (Vitamin B₆) 25 - 50 mg PO daily, to prevent the development of isoniazid-induced peripheral neuropathy.

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

Option	Total Duration (Months)	Initial Phase		Continuation Phase		Comments
		Drugs	Interval & Dose # (minimal duration)	Drugs	Interval & Dose # (minimal duration)	
1	6	Isoniazid Rifampin Pyrazinamide Ethambutol	Daily DOT for 40 doses (8 wks)	Isoniazid Rifampin	Daily DOT for 90 doses (18 wks) OR Twice-weekly DOT for 36 doses (18 wks) OR Thrice-weekly DOT for 54 doses (18 wks)	Regimen must be directly observed. Continue ethambutol until susceptibility to isoniazid and rifampin is demonstrated.
2*	6	Isoniazid Rifampin Pyrazinamide Ethambutol	Daily DOT for 10 doses (2 wks), then twice-weekly DOT for 12 doses (6 wks)	Isoniazid Rifampin	Twice-weekly DOT for 36 doses (18 wks)	Regimen must be directly observed. Include ethambutol in initial phase. After the initial phase, continue ethambutol until susceptibility to isoniazid and rifampin is demonstrated.

NOTE: Daily DOT = 5 days/week (Monday through Friday). Self-administered doses (including those on weekends) will not be counted toward the total doses.

NOTE: Pyridoxine (Vitamin B₆) 25- 50 mg/daily should be added to all regimens to prevent development of isoniazid-induced peripheral neuropathy.

***NOTE: Option 2 should NOT be used for patients with HIV infection, cavitary pulmonary TB, disseminated TB, vertebral TB or for patients who have co-morbid medical conditions such as diabetes mellitus, end-stage renal disease or liver disease.**

NOTE: Split dosing should be avoided.

NOTE: 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.

NOTE: Refer to current drug reference or drug package insert for a complete list of adverse drug reactions and drug interaction.

Table 2: First-Line TB Drugs

Drugs	Adult Dose based on body weight in kilograms (kg)*			Adverse Reactions
	Daily	Twice-Weekly	Thrice-Weekly	
Isoniazid	300 mg (5 mg/kg Maximum Dose 300 mg)	900 mg (15 mg/kg Maximum Dose 900 mg)	900 mg (15 mg/kg Maximum Dose 900 mg)	<ul style="list-style-type: none"> • Gastrointestinal (GI) upset • Liver enzyme elevation • Hepatitis • Peripheral neuropathy • Mild effects on central nervous system • Drug interactions
Rifampin	600 mg (10 mg/kg Maximum Dose 600 mg)	600 mg (10 mg/kg Maximum Dose 600 mg)	600 mg (10 mg/kg Maximum Dose 600 mg)	<ul style="list-style-type: none"> • Orange discoloration of body fluids and secretions • Drug interactions • GI upset • Hepatitis • Bleeding problems • Influenza-like symptoms • Rash
Pyrazinamide**	40-55 kg: 1000 mg 56-75 kg: 1500 mg 76+ kg: 2000 mg	40-55 kg: 2000 mg 56-75 kg: 3000 mg 76+ kg: 4000 mg	40-55 kg: 1500 mg 56-75 kg: 2500 mg 76+ kg: 3000 mg	<ul style="list-style-type: none"> • 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: 2000 mg 56-75 kg: 2800 mg 76+ kg: 4000 mg	40-55 kg: 1200 mg 56-75 kg: 2000 mg 76+ kg: 2400 mg	<ul style="list-style-type: none"> • Optic neuritis

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

** Calculate **pyrazinamide and ethambutol** doses **using actual** body weight. **NOTE:** Round up fractions of a dose to the nearest whole number. Obese clients (**BMI over 30**) are considered complicated cases **and dosing should be determined by district contract TB physician.**

Directly Observed Therapy (DOT) is mandatory.

NOTE: Refer to current drug reference or drug package insert for a complete list of adverse drug reactions and drug interactions.

Note: Ethambutol and pyrazinamide dosage adjustment may be needed if there is renal impairment. Patients with estimated creatinine clearance less than 50 ml/min or those with end-stage renal disease on dialysis are considered complicated cases and dosing should be determined by district contract TB physician.

CLIENT EDUCATION/COUNSELING

Education/communication should use methods adapted to client's cultural and linguistic background. Provide education to the client 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://www.health.state.ga.us/programs/tb/phclinicforms.asp>
 - **Transmission of Tuberculosis**
 - **Differences between latent TB infection (LTBI) and active TB disease**
 - **Progression of LTBI to active TB disease**
 - **Signs and symptoms of TB disease**
 - **Importance of HIV testing**
 - **Respiratory isolation and use of masks**
 - **Infectious period**
 - **Importance of chemotherapy as prescribed**
 - **Side effects and adverse medication reactions**
 - **Directly Observed Therapy**
 - **Importance of regular medical assessments**
 - **Importance of contact investigation**
2. The rationale for using an alternative or back-up method of birth control (e.g., copper-bearing IUD such as ParaGard, condoms, diaphragm) is that when rifampin is prescribed, it reduces effectiveness (degree depending on method) of combined oral contraceptives, progestin-only oral contraceptives, levonorgestrel implants, Depo-Provera, patch and ring. Advise condom back-up. (Table 4 on page **6.14** – Drug Interactions - Rifampin).
3. The client's immunization status. Assess and administer vaccines indicated according to the current Advisory Committee on Immunization Practices (ACIP) childhood or adult immunization schedule. **Although no data exist regarding whether measles, varicella or live varicella vaccine exacerbates TB, vaccination is not recommended for persons who have untreated active TB.** 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://www.health.state.ga.us/programs/immunization/publications.asp>

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 substance abuse known or suspected, refer for appropriate counseling.

FOLLOW-UP

1. Continued client management/follow-up by a case management team comprised of the client, nurse, physician and others determined by an individual needs assessment. **Refer to *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 <http://www.health.state.ga.us/programs/tb/phclinicforms.asp>**
2. After the nursing assessment, the Public Health Nurse (PHN) will use the **“Case Management Timeline – A Tracking Form for TB Medical Records”** located on the TB web pages at <http://www.health.state.ga.us/programs/tb/phclinicforms.asp> **to determine documents to forward for review by the district TB coordinator, the district’s contract physician and the state office. The district’s TB Coordinator will forward pertinent records to the state office, including (but not limited to) the following:**
 - a. Complete health history and pertinent physical findings.
 - b. Hospital discharge summaries (if available).
 - c. Treatment assessment and plan for DOT.
 - d. All other pertinent clinical data (e.g., prior chest x-rays, if available, and lab work).
3. **Review the respiratory isolation status for the client. All 3 of the following criteria must be met in order for isolation to be discontinued:**
 - a. **Client has three consecutive negative AFB sputum smear results**
 - b. **Client has received standard anti-tuberculosis treatment for a minimum of two weeks**
 - c. **Client has demonstrated clinical improvement**

During the initial treatment, sputum may be collected frequently in order to expedite meeting these criteria. There

must be a minimum of 8 hours between collection times if two samples are obtained on the same day. Early morning collection time is highest yield for detecting *Mtb*.

4. Monitor client(s) monthly for adverse drug reactions, drug-drug interactions, drug-food interactions, drug-lab interactions, infectious status, and clinical and bacteriologic response to therapy (see **Tables 3, 4 and 5 on pages 6.13 – 6.16** for drug interactions).
5. Provide HIV test results with post-test counseling to client and, if positive, appropriate referrals to HIV care. Seek confirmation that client kept referral appointment for HIV care.
6. Conduct a contact investigation following 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) to include:
 - a. The initial interview of the index **client** should be done by the PHN or designee (e.g., Communicable Disease Specialist) for all cases and suspects in the hospital (preferred) within one to three working days of health department notification. The follow-up interview should occur 1-2 weeks later, preferably in the **client's** home.
 - b. Start screening with high priority contacts in home, work, school and social environments. High priority contacts would be those persons with the greatest intensity, frequency and duration of exposure to the person who has infectious TB. Take into consideration risk factors (see item c immediately below) as well as exposure in determining high priority contacts. **NOTE:** High-priority contacts should be examined within seven working days. Medium priority contacts should be examined within fourteen calendar days. Low priority contacts should be examined within thirty calendar days.
 - c. High priority contacts who are considered a medical risk should be examined immediately regardless of initial TST **or IGRA**. Persons at particularly high risk of developing TB disease once infected with *M. tuberculosis* include: children less than 5 years of age and persons with immune systems compromised by HIV infection, immunosuppressive 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). Those contacts should have a chest x-ray and be placed on isoniazid if the chest x-ray is negative for active TB disease for window period treatment. **For HIV infected persons, treatment is continued for a full course.**
- d. Expand the contact investigation if there is evidence of recent transmission such as a higher than expected infection rate in high priority contacts, a secondary case of TB disease, infection in a child less than five years, or a converter.
 - e. Contact information should be entered on the *TB Contact Investigation Report Form* (Form #3126) and promptly entered into SENDSS.
7. **Collect sputum specimens for AFB smear and culture weekly to monitor the patient's response to therapy and to determine the appropriate length of treatment until conversion to negative culture is documented.** Obtain a sputum specimen for AFB smear and culture at **60 days after treatment initiation** to identify clients at increased risk for relapse. **If the culture at 60 days (2 months) after treatment initiation is still positive, refer treatment to the contract physician. Obtain** a monthly sputum specimen for AFB culture **even** after client is culture negative. **If the client is unable to produce sputum, document the attempt to collect sputum.**
8. Perform the following blood chemistry tests monthly to monitor reactions to TB drugs: AST (SGOT), ALT (SGPT), bilirubin, alkaline phosphatase and CBC with platelets. Perform serum uric acid and serum creatinine monthly 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, abnormal kidney function).
9. Discontinue the isoniazid or rifampin and report immediately to the consulting physician if any of the following occur:
- a. AST/ALT levels equal to or greater than 3 times the upper limit of normal in the presence of symptoms of adverse events.
 - b. AST/ALT levels equal to or greater than 5 times the upper limit of normal in an asymptomatic client.
 - c. Client reporting symptoms of adverse reactions.

10. Monitor the vision of clients taking ethambutol by providing vision checks monthly, including visual acuity and red/green color discrimination.
11. Use incentives and enablers to enhance adherence to therapy. These may be as simple as offering a cup of coffee and talking with a client who is waiting in the clinic, or as complex as providing food and housing for a homeless client.
12. Observe the client for isoniazid-induced peripheral neuropathy during the course of therapy and report to the delegating physician.
13. Treatment completion is defined by the number of doses taken as well as the duration of treatment. The number of doses required is listed in Table 1, page **6.5**.

CONSULTATION

Consult with the consulting physician:

1. Before changing to the continuation phase of Regimen Options (1) or (2) (see Table 1, page **6.5**), and regarding complications that would require reevaluation of the client and possible new treatment recommendations.
2. If susceptibility results show resistance to TB drug.
3. If the client remains symptomatic or smear or culture positive after two months.
4. If the client's HIV test result is positive.
5. If the client refuses HIV testing.
6. To discuss abnormal laboratory test results.
7. If the client is not compliant with DOT.

REFERRAL

1. Refer clients for other medical and social services as needed, particularly alcohol or drug abuse treatment, **diabetes care (if**

hemoglobin A1C is 6.5% or higher) and HIV care. You may contact the TB state office Social Services Provider for assistance with these issues.

2. **If any of the following conditions are present or develop, the case is considered a complicated TB case and TB treatment must be ordered by the district contract TB physician**
 - a. **Children from birth through 15 years**
 - b. **Extrapulmonary TB**
 - c. **Currently pregnant or breast-feeding**
 - d. **Known history of infection or exposure to multiple drug resistant (MDR) M. tuberculosis, or any drug resistance on susceptibility testing**
 - e. **Known HIV infection**
 - f. **Other new and/or complicated acute or chronic medical conditions including (but not limited to): diabetes, renal insufficiency with estimated creatinine clearance less than 50 ml/min., end-stage renal disease on hemodialysis**
 - g. **BMI greater than 30**
 - h. **Known allergies to anti-tuberculosis drugs**
 - i. **Treatment with once-weekly isoniazid and rifapentine during the continuation phase**
 - j. **Decision to extend the continuation phase longer than four months (e.g., sputum culture collected 60 days (2 months) after treatment initiation is positive).**
3. Refer client to a licensed dietitian (LD), if indicated. This will be especially important if the client has a history of drug or alcohol abuse, is breast-feeding, is HIV-infected, has GI side effects from TB drugs or if desirable weight is not maintained.
4. Refer to the Georgia TB Reference Guide (current edition) for treatment timelines.

Table 3: TREATMENT OF TB - DRUG INTERACTIONS (Format 1)

DRUG INTERACTIONS – RIFAMPIN

<u>Drug A</u>	<u>Rifampin Effects on Drug A</u>
Anticoagulants (warfarin, coumadin)	↓ serum concentration
Cardiac glycosides (digoxin)	↓ serum concentration
Sulfonylureas (e.g. glipizide, glyburide, glimepiride)	↓ serum concentration
Thiazolidinediones (e.g. rosiglitazone, pioglitazone)	↓ serum concentration
Oral contraceptives, contraceptive implants, patch, ring, Depo-Provera	↓ efficacy
Fluconazole, Voriconazole, Itraconazole	↓ serum concentration
Corticosteroids	↓ serum concentration
Narcotics/analgesics (methadone)	↓ serum concentration
Atovaquone (Mepron)	↓ serum concentration
Dapsone	↑ clearance
Cyclosporine	↓ serum concentration
Quinidine	↓ peak serum concentration
Protease inhibitors	↓ serum concentration
Lamotrigine (Lamictal)	↓ serum concentration
Phenytoin (Dilantin)	↓ serum concentration
Valproic acid and derivatives (depakene, depakote)	↓ serum concentration
Buspiron (buspar)	↓ serum concentration
Thyroid hormone replacement	↓ serum concentration

DRUG INTERACTIONS – ISONIAZID

<u>Drug A</u>	<u>Isoniazid Effects on Drug A</u>
Diazepam (valium)	↓ clearance ↑ half life (time to excreted)
Phenytoin (Dilantin)	↑ plasma concentration ↑ toxicity
Carbamazepine (tegretol)	↑ plasma concentration ↑ toxicity
Citalopram (Celexa)	↑ plasma concentration ↑ toxicity

NOTE: Refer to current drug reference or drug package insert for a complete list of adverse drug reactions and drug interactions.

Table 4: TREATMENT OF TB - DRUG INTERACTIONS (Format 2)

DRUG INTERACTIONS – RIFAMPIN/RIFAPENTINE

Rifampin or Rifapentine plus...	
Adefovir	Increases risk of side effects.
Amprenavir	Should not be used together.* Significantly decreases amprenavir levels in blood.
Anticoagulants	May decrease effectiveness of anticoagulants.
Atovaquone	Decreases atovaquone levels by 50% in blood.
AZT	May decrease AZT levels in blood.
Barbiturates	May decrease effectiveness of barbiturates.
Clarithromycin	Lowers blood levels of Clarithromycin
Corticosteroids	May decrease corticosteroid levels in blood.
Cyclosporine	May decrease cyclosporine levels in blood.
Dapsone	Decreases dapsone levels by 7- to 10-fold in blood.
Delavirdine	Should be taken together otherwise delavirdine levels in blood significantly decreased.
Diazepam	May decrease effectiveness of diazepam.
Digitalis	May decrease effectiveness of digitalis.
Disopyramide	May decrease effectiveness of disopyramide.
Efavirenz	Decreases efavirenz levels by 26% in blood.
Estrogen	May decrease effectiveness of estrogen.
Ethinyl Estradiol (birth control pills)	May decrease ethinyl estradiol levels in blood.
Fluconazole	Decreases fluconazole levels by 23% in blood.
Halothane	May increase risk of liver toxicity.
Indinavir	May increase rifampin levels in blood. Should not be used together.*
Isoniazid	May increase risk of liver toxicity.
Itraconazole	May decrease itraconazole levels in blood.
Lopinavir/ritonavir	Decreases lopinavir levels by 75% in blood. Should not be used together.
Methadone	May decrease effectiveness of methadone.
Mexilitine	May decrease effectiveness of mexilitine.
Nelfinavir	Decreases nelfinavir levels by 82% in blood. Should not be used together.*
Nevirapine	May affect rifampin and/or nevirapine levels in blood.
Probenecid	Increases rifampin levels in blood.
Progesterone	May decrease effectiveness of progesterone.
Quinidine	May decrease quinidine levels in blood.
Ritonavir	Decreases ritonavir levels by 35% in blood.
Theophylline	May decrease theophylline levels in blood.

Rifampin or Rifapentine plus...	
Verapamil	May decrease effectiveness of verapamil.
Voriconazole	May decrease voriconazole levels in blood.

* The information on interactions with rifampin and **HIV antiretroviral therapy (ART)** is constantly changing. Consult with the consulting physician/contract physician. In general, only certain **HIV medications** can be used and rifampin may be replaced by rifabutin. Rifabutin is in the formulary at the state pharmacy.

NOTE: Refer to current drug reference or drug package insert for a complete list of adverse drug reactions and drug interactions.

Table 5: DRUG INTERACTIONS – ISONIAZID

Isoniazid plus...	
Alcohol	May increase risk of isoniazid associated hepatitis.
Antacids	Should be taken two hours apart otherwise isoniazid will have no effect.
Carbamazepine	Decreases carbamazepine metabolism.
Cycloserine	May increase risk of central nervous system toxicity.
Ethionamide	May increase risk of encephalopathy (dysfunction of the brain) and may increase isoniazid levels in blood.
Phenytoin	Decreases phenytoin metabolism.

NOTE: Refer to current drug reference or drug package insert for a complete list of adverse drug reactions and drug interactions.

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STANDARD NURSE PROTOCOL FOR LATENT TUBERCULOSIS INFECTION (LTBI)

DEFINITION

Latent tuberculosis infection (LTBI) means that a person has been infected with *Mycobacterium tuberculosis* but has no clinical or radiographic evidence of TB. 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.

Candidates for treatment of LTBI include:

1. Persons in the following high-risk groups should be given treatment for LTBI if they have positive skin test results of equal to or greater than 5 mm **or if they have a positive interferon gamma release assay (IGRA) result:**
 - a. HIV-positive persons.
 - b. Recent contacts to a TB case.
 - c. Persons with fibrotic changes on chest radiograph consistent with old TB.
 - d. Persons with organ transplants and other immunosuppressed persons (those receiving the equivalent of equal to or greater than 15 mg daily of prednisone for 1 month or longer).

2. Persons in the following high-risk groups should be considered for treatment of LTBI if their reaction to the tuberculin skin test is equal to or greater than 10 mm **or if they have a positive interferon gamma release assay (IGRA) result:**
 - a. Recent arrivals (less than 5 years) from 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 facilities for the elderly, homeless shelters, residential facilities for AIDS clients, 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. tuberculosis* within the past two years, diabetes, hematologic or reticuloendothelial malignancies, chronic renal failure, post-gastrectomy, silicosis, immunosuppressive therapy, chronic malabsorption).

- syndromes or 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. Children less than 5 years of age, or children and adolescents exposed to adults in high-risk groups.
3. Persons with no risk factors for TB should be considered for treatment of LTBI if their reaction to the tuberculin skin test is greater than or equal to 15 mm **or if they have a positive interferon gamma release assay (IGRA) result.**

Treatment of LTBI might NOT be indicated for:

1. Persons at increased risk for adverse reactions to isoniazid and persons for whom isoniazid is contraindicated.
2. Persons who cannot tolerate isoniazid or rifampin.
3. Persons likely to be infected with drug-resistant *M. tuberculosis*.
NOTE: They should be referred to the consulting physician.
4. Persons who are not likely to complete a course of treatment for LTBI (e.g., some homeless persons or migrant farm workers).

Treatment of LTBI might NOT be completed on:

1. **Persons who are a contact to a TB suspect later found not to have TB. NOTE: They should be referred to the consulting physician.**

ETIOLOGY

The agent is the *Mycobacterium tuberculosis* complex.

SUBJECTIVE

1. May have a history of known exposure to TB
2. **The absence** of risk factors indicating special precautions needed for persons receiving isoniazid therapy. **These risk factors include:**
 - a. Concurrent use of any other medications on a long-term basis, or medications that may cause interactions
 - b. Alcohol abuse
 - c. Previous discontinuation of isoniazid because of side effects
 - d. Chronic liver disease

- e. Peripheral neuropathy
- f. Pregnancy
- g. Injection drug abuse

- 3. No known allergies to anti-tuberculosis drugs
- 4. Absence of symptoms of TB

OBJECTIVE

- 1. A positive Mantoux tuberculin skin test **or a positive interferon gamma release assay (IGRA) result** and no clinical symptoms of active disease

AND

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

AND

- 3. Absence of clinical signs of TB, both pulmonary and extra-pulmonary
- 4. **If signs and symptoms of TB disease are evident, client should have 3 consecutive negative sputum smears and cultures with evaluation by a clinician before starting treatment for LTBI.**

ASSESSMENT

- 1. Latent tuberculosis infection (LTBI) (without signs/symptoms of tuberculosis disease)
- 2. No contraindications to isoniazid or rifampin
- 3. No history of documented infection from or exposure to drug-resistant *M. tuberculosis* source case

PLAN

DIAGNOSTIC STUDIES

- 1. If documented tuberculin skin test results (including millimeters [mm] of induration), **or a positive interferon gamma release assay (IGRA) result** cannot be verified, perform a Mantoux tuberculin skin test. **Vaccination with live viruses may interfere with tuberculin skin test reactions. For persons scheduled to receive a tuberculin skin test, testing should be done as follows: Either on the same day as vaccination with live-virus vaccine or 4-6 weeks after the administration of the live-virus vaccine. At least one month after smallpox vaccination.**

2. Baseline weight.
3. Collect blood to obtain baseline measurements for the following lab tests:
 - a. AST (SGOT), ALT (SGPT), alkaline phosphatase and bilirubin.
 - b. All individuals will be tested for HIV using the opt-out approach. Consent is inferred unless client declines testing.
 - c. Hepatitis B and C profile, if indicated (**risk groups below**):
 - **Men who have sex with men**
 - **Individuals diagnosed with a sexually transmitted disease (STD)**
 - **Illicit drug users (injecting, inhaling, snorting, pill popping)**
 - **Sex contacts or close household members of a person infected with Hepatitis B or C**
 - **Persons born in countries where hepatitis B is common (Asia, Africa, South America, Pacific Islands, Eastern Europe, and the Middle East)**
 - **Individuals born to parents who have emigrated from countries where hepatitis B is common (see above)**
 - d. **Baseline complete blood count with platelets for patients on the Isoniazid-rifapentine regimen or rifampin regimen.**
4. Pregnancy test, if indicated.

NOTE: The baseline lab measurements are not mandatory for children less than 16 years of age, unless a complicating medical condition (e.g., HIV, liver disease, renal disease, cardiac disease) or lifestyle is known or suspected.

THERAPEUTIC

PHARMACOLOGIC

Refer to options, dosages and interactions of isoniazid, rifampin and isoniazid/rifapentine in **Tables A – I on pages 6.27 - 6.36.**

1. Order medication for treatment in children and adults from drug stock and send copies of the drug orders to the District Pharmacist/Drug Coordinator.
2. Add pyridoxine (Vitamin B₆) 25-50 mg PO daily for adults on isoniazid, to prevent the development of isoniazid - induced peripheral neuropathy (see **TABLE A on page 6.27**).

NOTE: Directly Observed Therapy (DOT) is REQUIRED for all clients less than 5 years of age, HIV infected persons, clients on ANY intermittent dosing regimen and clients on the combined isoniazid and rifapentine regimen. Directly Observed Therapy (DOT) is **strongly** recommended for all children up to the age of 15 years. DOT should also be considered for clients who are at high risk for TB (**e.g., close contacts, immunocompromised persons, converters**) and whose adherence to LTBI therapy is questionable.

NOTE: When using the Isoniazid/Rifapentine regimen, review the CDC guidelines at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_e%0d%0a. Use the "Isoniazid/Rifapentine Reporting and DOT" form located at <http://health.state.ga.us/programs/tb/phclinicforms.asp>

CLIENT EDUCATION/COUNSELING

Education/communication should use methods adapted to client's cultural and linguistic background. Provide education to the client and his/her family regarding the following:

1. The rationale for treatment of LTBI and the importance of attending regularly scheduled clinic appointments.
2. The difference between "latent TB infection" (LTBI) and "TB disease" and what a "positive skin test" means.
3. The signs and symptoms of TB disease and the need to report immediately if anyone has these symptoms.
4. The symptoms of adverse reactions to isoniazid, **rifampin, or isoniazid/rifapentine** including: GI disturbances (anorexia, heartburn, nausea, vomiting, gas, cramps, diarrhea), hepatitis

(loss of appetite, persistently dark urine, yellowish skin/sclera, malaise, unexplained fever for three or more days, abdominal tenderness) and peripheral neuropathy (see **Table C on page 6.28**). Advise the client to report immediately to the Public Health Nurse or clinician if any such symptoms occur during treatment.

5. The relationship between HIV infection and TB infection and the importance of HIV testing for all TB-infected individuals.
6. The rationale for using an alternative or back-up method of birth control (e.g., copper-bearing IUD such as ParaGard, condoms, diaphragm) is that when rifampin is prescribed, it reduces effectiveness (degree depending on method) with combined oral contraceptives, progestin-only oral contraceptives, levonorgestrel implants, Depo-Provera, patch and ring. Advise condom back-up.
7. The client's immunization status. Assess and administer vaccines indicated according to the current Advisory Committee on Immunization Practices (ACIP) childhood or adult immunization schedule. 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 on line at <http://www.health.state.ga.us/programs/immunization/publications.asp>
8. If smoker or tobacco user, refer to a local cessation program and/or the Georgia Tobacco Quit Line, 1-877-270-STOP (7867).
9. If substance abuse known or suspected, refer for appropriate counseling.

FOLLOW-UP

1. At least once a month, evaluate for:
 - a. Adherence to the prescribed regimen.
 - 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).
 - c. Symptoms of neurotoxicity such as paresthesia of hands or feet.
 - d. Maintenance of desirable weight.
 - e. Adverse effects of prescribed regimen.

2. At follow-up visits, ask clients about adherence to therapy.
3. Provide the HIV test result with post-test counseling and, if the test is positive, appropriately refer for HIV care. Seek confirmation that client kept referral appointment for HIV care.
4. **All clients on LTBI therapy should be assessed for the presence of symptoms of hepatotoxicity at every encounter. Clients considered at risk of hepatotoxicity should have an AST and ALT done monthly. Those considered at risk include:**
 - a. **Those with admission of frequent past or any current alcohol use**
 - b. **Those with admission of past or current IV drug use**
 - c. **HIV**
 - d. **Hepatitis B or C**
 - e. **Pregnancy / postpartum state**
5. Observe for isoniazid-induced peripheral neuropathy during the course of isoniazid therapy. When peripheral neuropathy is present and/or persists, report to the consulting physician.
6. Pregnant women, particularly African-American and Hispanic women, may be at increased risk for fatal hepatitis associated with isoniazid, according to some reports. This risk may be increased during the postpartum period. These clients should be closely monitored for adverse reactions throughout the course of treatment. **The risk of hepatitis from isoniazid in pregnant/post-partum women does NOT preclude treatment of LTBI if these women are at extremely high risk for developing active TB (e.g., close contact, HIV-infected, or with documented recent infection or conversion).**
7. Discontinue the isoniazid, rifampin **or isoniazid/rifapentine** and report immediately to the consulting physician if any of the following occur:
 - a. AST/ALT levels equal to or greater than 3 times the upper limit of normal in the presence of symptoms of adverse events.
 - b. AST/ALT levels equal to or greater than 5 times the upper limit of normal in an asymptomatic client.
 - c. If the client reports any symptoms of adverse reactions obtain AST/ALT immediately and notify consulting physician.

- d. Any hospital admissions or deaths due to adverse reactions are to be reported immediately to the State TB Program.
4. A clinical symptom screen is required for all clients who have a lapse in treatment. A repeat chest x-ray/evaluation is required for clients who are symptomatic or who have had a lapse in therapy for LTBI for two months or more.
5. Treatment completion is defined by the number of doses taken as well as the duration of treatment. The number of doses required is listed in **Tables A and B, pp. 6.27 – 6.28.**

CONSULTATION

Consult with the TB Program medical consultant or consulting physician:

1. Regarding any complications of treatment for LTBI with clients placed on Isoniazid, rifampin **or Isoniazid/rifapentine** (see **Tables A - F on pages 6.27 – 6.33** for drug interactions, drug adverse reactions and drug monitoring).
2. If a client's HIV test result is positive, or if a client at risk refuses HIV testing.
3. About any abnormal lab test results.

REFERRAL

1. Refer clients for other medical and social services as needed, particularly alcohol or drug abuse treatment and HIV care.
2. Refer all clients with complications (pregnant women, breast-feeding women, clients with acute or chronic conditions, clients exposed to drug-resistant TB, HIV-infected clients taking protease inhibitors) to the consulting physician.
3. **Refer children aged 2 through 11 years of age 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 mo of daily Isoniazid.**

Table A: TREATMENT OF LTBI - RECOMMENDED DRUG REGIMENS FOR ADULTS (persons 16 and over)

Drug	Interval and Duration	Adult Dosage	Criteria for Completion	Comments
Isoniazid*	Daily self-adm**for 9 months Daily DOT for 9 months ♦ Twice-weekly DOT for 9 months	300 mg PO (5 mg/kg - Maximum Dose 300 mg) 300 mg PO (5 mg/kg - Maximum Dose 300 mg) 900 mg PO (15 mg/kg - Maximum Dose 900 mg)	270 doses within 12 months 190 doses within 12 months 76 doses within 12 months	In HIV-infected clients, isoniazid may be taken concurrently with nucleoside reverse transcriptase inhibitors (NRTIs) , protease inhibitors, or non-nucleoside reverse transcriptase inhibitors (NNRTIs) . <i>DOT must be used with twice-weekly dosing.</i> NOTE: Not recommended for HIV-infected clients.
Rifampin	Daily self-adm** for 4 months (18 weeks) Daily DOT for 4 months (18 weeks) ♦	600 mg PO (10 mg/kg - Maximum Dose 600 mg) 600 mg PO (10 mg/kg - Maximum Dose 600 mg)	120 doses within 6 months 90 doses within 6 months	Rifampin therapy may be used for persons who are contacts of clients with isoniazid-resistant, rifampin susceptible TB but may also be chosen for other persons with LTBI.
Isoniazid* and Rifapentine	Once weekly by DOT for 12 doses	Isoniazid: 15 mg/kg PO (rounded up to the nearest 50 or 100 mg); 900 mg PO maximum Rifapentine: 10.0-14.0 kg 300 mg PO 14.1-25.0kg 450 mg PO 25.1-32.0 kg 600 mg PO 32.1-49.9 kg 750 mg PO Equal to or over 50.0 kg 900 mg (maximum dose) PO	11 doses within 16 weeks (doses may be given no more frequently than every 72 hours)	Isoniazid and rifapentine is recommended as an equal alternative to 9 months of daily self-administered Isoniazid for treating LTBI in otherwise healthy patients aged 12 years and older at high risk for developing active TB: close contacts, recent converters, HIV infected (NOT on antiretrovirals) and those with old healed TB on chest x-ray. Isoniazid and rifapentine can also be used in situations where it offers practical advantages or for individuals unlikely to complete 9 months of daily isoniazid. Isoniazid and rifapentine is NOT recommended for the following patients: children age less than 2 years; HIV infected persons receiving antiretroviral treatment; pregnant women or women expecting to become pregnant during treatment; and patients who have LTBI with presumed isoniazid or rifampin resistance.

* 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.

** Daily self-administered = 7 days/week

♦ Daily DOT = 5 days/week (Monday through Friday) NOTE: One month is 4.3 week

NOTE: Formula used to convert pounds to kilograms: Divide pounds by 2.2 to get kilograms. Example: Client weighs 154 pounds ÷ 2.2 = 70 kilograms.

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.

Table B: TREATMENT OF LTBI - RECOMMENDED DRUG REGIMENS FOR CHILDREN (from birth through 15 years)

Drug	Interval and Duration	Pediatric Dosage*	Criteria for Completion	Comments
Isoniazid*	Daily self-adm** for 9 months (39 weeks)	10-15 mg/kg PO (Maximum Dose 300mg)	270 doses within 12 months	Isoniazid for 9 months is the preferred regimen children under 12. DOT must be used with twice-weekly dosing. NOTE: Not recommended for HIV-infected clients.
	Daily DOT♦ for 9 months (39 weeks)	10-15 mg/kg PO (Maximum Dose 300mg)	190 doses within 12 months	
	Twice-Weekly DOT for 9 months (39 weeks)	20-30 mg/kg PO (Maximum Dose 900mg)	76 doses within 12 months	
Rifampin	Daily self-adm** for 6 months (26 weeks)	10-20 mg/kg PO (Maximum Dose 600mg)	180 doses within 9 months	Rifampin therapy may be used for persons who are contacts of clients with isoniazid-resistant, rifampin susceptible TB but may also be chosen for other persons with LTBI.
	Daily DOT♦ for 6 months (26 weeks)	10-20 mg/kg PO (Maximum Dose 600mg)	130 doses within 9 months	
Isoniazid* and Rifapentine	Once weekly by DOT for 12 doses	Isoniazid: 15 mg/kg PO rounded up to the nearest 50 or 100 mg; 900 mg PO maximum Rifapentine: 10.0-14.0 kg 300 mg PO 14.1-25.0kg 450 mg PO 25.1-32.0 kg 600 mg PO 32.1-49.9 kg 750 mg PO Equal to or over 50.0 kg 900 mg (Maximum dose) PO	11 doses within 16 weeks (doses may be given no more frequently than every 72 hours)	Isoniazid and Rifapentine is recommended as an equal alternative to 9 months of daily self-administered isoniazid for treating LTBI in otherwise healthy patients aged 12 years and older at high risk for developing active TB: close contacts, recent converters, HIV infected (NOT on antiretrovirals) and those with old healed TB on chest x-ray. Refer to the contract physician children aged 2 through 11 years of age 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 mo of daily Isoniazid. Isoniazid and Rifapentine is NOT recommended for the following patients: children age less than 2 years; HIV infected persons receiving antiretroviral treatment; pregnant women or women expecting to become pregnant during treatment; and patients who have LTBI with presumed Isoniazid or rifampin resistance.

**Daily self administrated (adm) = 7 days/week ♦ Daily DOPT = 5 days/week (Monday through Friday). NOTE: One month is 4.3 weeks.

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

NOTE: Directly Observed Therapy (DOT) is REQUIRED for all clients less than 5 years of age, clients on ANY intermittent dosing regimen (including the combined isoniazid and rifapentine regimen). Directly Observed Therapy (DOT) is recommended for all children up to the age of 15 years.

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.

Table C: TREATMENT OF LTBI - DRUG ADVERSE REACTIONS AND MONITORING

Drug	Adverse Reactions	Monitoring	Comments
Isoniazid	Gastrointestinal (GI) upset, hepatic enzyme elevations, hepatitis, peripheral neuropathy, mild effects on central nervous system, drug interactions	Baseline measurements of AST for adults. Repeat measurements: – if baseline results are abnormal – if client is at high-risk for adverse reactions – if client has symptoms of adverse reactions	Hepatitis risk increases with age and alcohol consumption. 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*	Complete blood count, platelets and liver function tests. Repeat measurements if: – baseline results are abnormal – client has symptoms of adverse reactions	Hepatitis risk increases with age and alcohol consumption.

* Hypersensitivity reaction to rifamycins (rifampin or rifapentine):

Hypersensitivity reactions may include a flu like syndrome (e.g. fever, chills, headaches, dizziness, 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 (Format 1)

DRUG INTERACTIONS – RIFAMYCINS (Rifampin, Rifapentine*)

* Rifapentine has interactions similar to rifampin. It induces cytochromes P4503A4 and P4502C8/9 (less than rifampin)

<u>Drug A</u>	<u>Rifampin Effects on Drug A</u>
Anticoagulants (warfarin, coumadin)	↓ serum concentration
Cardiac glycosides (digoxin)	↓ serum concentration
Sulfonylureas (e.g. glipizide, glyburide, glimepiride)	↓ serum concentration
Thiazolidinediones (e.g. rosiglitazone, pioglitazone)	↓ serum concentration
Oral contraceptives, contraceptive implants, patch, ring, Depo-Provera	↓ efficacy
Fluconazole, Voriconazole, Itraconazole	↓ serum concentration
Corticosteroids	↓ serum concentration
Narcotics/analgesics (methadone)	↓ serum concentration
Atovaquone (Mepron)	↓ serum concentration
Dapsone	↑ clearance
Cyclosporine	↓ serum concentration
Quinidine	↓ peak serum concentration
Protease inhibitors	↓ serum concentration
Lamotrigine (Lamictal)	↓ serum concentration
Phenytoin (Dilantin)	↓ serum concentration
Valproic acid and derivatives (depakene, depakote)	↓ serum concentration
Bupirone (buspar)	↓ serum concentration
Thyroid hormone replacement	↓ serum concentration

DRUG INTERACTIONS – ISONIAZID

<u>Drug A</u>	<u>Isoniazid Effects on Drug A</u>
Diazepam (Valium)	↓ clearance ↑ half life (time to excreted)
Phenytoin (Dilantin)	↑ plasma concentration ↑ toxicity
Carbamazepine (tegretol)	↑ plasma concentration ↑ toxicity
Citalopram (Celexa)	↑ plasma concentration ↑ toxicity

NOTE: Refer to current drug reference or drug package insert for a complete list of adverse drug reactions and drug interactions.

Table E: TREATMENT OF LTBI - DRUG INTERACTIONS (Format 2)

DRUG INTERACTIONS – RIFAMPIN/RIFAPENTINE

Rifampin or Rifapentine plus...	
Adefovir	Increases risk of side effects.
Amprenavir	Should not be used together.* Significantly decreases amprenavir levels in blood.
Anticoagulants	May decrease effectiveness of anticoagulants.
Atovaquone	Decreases atovaquone levels by 50% in blood.
AZT	May decrease AZT levels in blood.
Barbiturates	May decrease effectiveness of barbiturates.
Clarithromycin	Lowers blood levels of Clarithromycin
Corticosteroids	May decrease corticosteroid levels in blood.
Cyclosporine	May decrease cyclosporine levels in blood.
Dapsone	Decreases dapsone levels by 7- to 10-fold in blood.
Delavirdine	Should be taken together otherwise delavirdine levels in blood significantly decreased.
Diazepam	May decrease effectiveness of diazepam.
Digitalis	May decrease effectiveness of digitalis.
Disopyramide	May decrease effectiveness of disopyramide.
Efavirenz	Decreases efavirenz levels by 26% in blood.
Estrogen	May decrease effectiveness of estrogen.
Ethinyl Estradiol (birth control pills)	May decrease ethinyl estradiol levels in blood.
Fluconazole	Decreases fluconazole levels by 23% in blood.
Halothane	May increase risk of liver toxicity.
Indinavir	May increase rifampin levels in blood. Should not be used together.*
Isoniazid	May increase risk of liver toxicity.
Itraconazole	May decrease itraconazole levels in blood.
Lopinavir/ritonavir	Decreases lopinavir levels by 75% in blood. Should not be used together.
Methadone	May decrease effectiveness of methadone.
Mexilitine	May decrease effectiveness of mexilitine.
Nelfinavir	Decreases nelfinavir levels by 82% in blood. Should not be used together.*
Nevirapine	May affect rifampin and/or nevirapine levels in blood.
Probenecid	Increases rifampin levels in blood.
Progesterone	May decrease effectiveness of progesterone.
Quinidine	May decrease quinidine levels in blood.
Ritonavir	Decreases ritonavir levels by 35% in blood.
Theophylline	May decrease theophylline levels in blood.

Rifampin or Rifapentine plus...	
Verapamil	May decrease effectiveness of verapamil.
Voriconazole	May decrease voriconazole levels in blood.

* The information on interactions with rifampin and **HIV antiretroviral therapy (ART)** is constantly changing. Consult with the consulting physician/contract physician. In general, only certain **HIV medications** can be used and rifampin may be replaced by rifabutin. Rifabutin is in the formulary at the state pharmacy.

NOTE: Refer to current drug reference or drug package insert for a complete list of adverse drug reactions and drug interactions.

Table F: DRUG INTERACTIONS – ISONIAZID

Isoniazid plus...	
Alcohol	May increase risk of isoniazid associated hepatitis.
Antacids	Should be taken two hours apart otherwise isoniazid will have no effect.
Carbamazepine	Decreases carbamazepine metabolism.
Cycloserine	May increase risk of central nervous system toxicity.
Ethionamide	May increase risk of encephalopathy (dysfunction of the brain) and may increase isoniazid levels in blood.
Phenytoin	Decreases phenytoin metabolism.

NOTE: Refer to current drug reference or drug package insert for a complete list of adverse drug reactions and drug interactions.

Table G: PEDIATRIC DOSAGE - ISONIAZID IN CHILDREN AND ADOLESCENTS
DAILY DOSAGE OF ISONIAZID IN CHILDREN AND ADOLESCENTS

Child's Weight in lbs	Child's Weight in kg	Daily Dose (mg) 10-15 mg/kg
6 – 14	3 – 6	50
14.5 – 21	6.5 – 9.5	100
22 – 29	10 – 13	150
30 – 35	13.5 – 16	200
36 – 43	16.5 – 19.5	250
44 +	20 +	300

TWICE-WEEKLY DOSAGE OF ISONIAZID IN CHILDREN AND ADOLESCENTS

Child's Weight in lbs	Child's Weight in kg	Twice-weekly Dose (mg) 20-30 mg/kg
6.5 – 10	3 – 4.5	100 mg PO
11 – 14	5.0 – 6.0	150 mg PO
14.5 – 18	6.5 – 8.0	200 mg PO
18.5 – 21.5	8.5 – 9.5	250 mg PO
22 – 24	10.0 – 11	300 mg PO
25 – 29	11.5 – 13	350 mg PO
29.5 – 32	13.5 – 14.5	400 mg PO
33 – 35	15 – 16	450 mg PO
36 – 40	16.5 – 18.	500 mg PO
40.5 – 43	18.5 – 19.5	550 mg PO
44 – 48	20 – 21.5	600 mg PO
48.5 – 51	22 – 23	650 mg PO
52 – 54.5	23.5 – 24.5	700 mg PO
55 – 57.5	25 – 26	750 mg PO
58 – 62	26.5 – 28	800 mg PO
62.5 – 65	28.5 – 29.5	850 mg PO
66 +	30 +	900 mg PO

NOTE: Isoniazid Syrup should not be refrigerated (keep at room temperature). Isoniazid tablets can be crushed for oral administration. Isoniazid tablets are also scored.

Table H: PEDIATRIC DOSAGES - RIFAMPIN IN CHILDREN AND ADOLESCENTS
DAILY DOSAGE OF RIFAMPIN IN CHILDREN AND ADOLESCENTS

Child's Weight in lbs	Child's Weight in kg	Daily Dose (mg) 10-20 mg/kg
15 – 32	7 – 14.5	150
33 – 48.5	15 - 22	300
49 – 65	22.5 – 29.5	450
66 +	30 +	600

Table I: ISONIAZID and RIFAPENTINE DOSE AMOUNTS for CLIENTS (children and adults) prescribed weekly INH/Rifapentine for Treatment of Latent TB Infection

Client's Weight in lbs	Client's Weight in kg	Isoniazid Weekly dose (mg) 15 mg/kg	Rifapentine Weekly dose (mg) 20 mg/kg
22 – 29.3	10 – 13.3	200	300
29.4 – 30.9	13.4 – 14.0	250	300
31.0 – 36.6	14.1 – 16.6	250	450
36.7 – 44.0	16.7 – 20.0	300	450
44.1 – 51.4	20.1 – 23.3	350	450
51.5 – 55.0	23.4 – 25.0	400	450
55.1 – 58.8	25.1 – 26.7	400	600
58.9 – 66.0	26.8 - 30	450	600
66.1 – 70.5	30.1 – 32.0	500	600
70.6 – 73.3	32.1 – 33.3	500	750
73.4 – 80.9	33.4 – 36.7	550	750
81.0 – 88.0	36.8 - 40	600	750
88.1 – 95.5	40.1 – 43.3	650	750
95.6 – 102.9	43.4 – 46.7	700	750
103.0 – 110.0	46.8 – 49.9	750	750
110.1 – 117.4	50 – 53.3	800	900
117.5 – 124.9	53.4 – 56.7	850	900
125+	56.8+	900	900

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. This means a client of average weight (125 lbs or more) will need to take 3 tablets of Isoniazid and 6 tablets of Rifapentine. Clients need to be aware of the pill burden when offered this regimen.

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