

### A. Eligible clients

1. Clients with all of the following:
  - **May have** a history of exposure to TB.
  - CXR without findings of active TB disease.
  - No signs or symptoms suggestive of active TB disease.
  - A **positive** TST or IGRA result.
2. Clients with all of the following:
  - A history of exposure to TB.
  - CXR without findings of active TB disease.
  - No signs or symptoms suggestive of active TB disease.
  - A **negative** TST or IGRA result.
  - A contact to a TB case/suspect.

Should be considered for treatment (**window prophylaxis**) due to one of the following:

- Clients younger than 5 years of age.
- Immunosuppressed clients.  
Note: Even if repeat TST or IGRA testing administered >8 weeks after the end of exposure yields a negative result, a complete course of treatment for LTBI is recommended for close contacts who are **HIV positive** after a medical evaluation to exclude TB disease. A complete course of treatment for LTBI *should be considered* for other severely immune compromised individuals after a medical evaluation to exclude TB disease.

### B. Pretreatment evaluation

**Before beginning treatment for LTBI, active TB should be ruled out** by history, physical examination, CXR, and when indicated, bacteriologic studies. If patient is suspected of having active TB disease, see **ATTACHMENT #4: Nursing Management of Clients with or Suspected to have TB Disease (Pulmonary and/or Extrapulmonary Disease)**.

Note: If client has signs or symptoms of active TB disease, irrespective of CXR findings,

consult the authorizing physician before starting LTBI treatment

1. **Sputum examination is not indicated for most clients** being considered for treatment of LTBI.

**Exceptions:**

- Clients with CXR findings suggestive of prior, healed TB infection should have three consecutive sputum samples, obtained on different days, submitted for AFB smear and culture. Results of sputum smears and cultures must be negative before treatment for LTBI is started.
- HIV-infected clients with respiratory symptoms who are being considered for treatment of LTBI should have sputum specimens submitted for AFB smear and culture, even if the CXR is normal. If results of sputum smears and cultures are negative and respiratory symptoms can be explained by another etiology, then treatment for LTBI can be started. If bacteriologic results are negative but the activity or etiology of a radiographic abnormality is questionable, further evaluation should be undertaken. Treatment of LTBI should not be started until active TB has been excluded.

- C. **Chest X-ray** must be obtained and show no evidence of active TB disease before starting treatment for LTBI.

Note: It is recommended that clients up to age 18 have both posterior-anterior and lateral views; all other clients should have at least posterior-anterior views. Other views or additional studies should be done only by order of the authorizing physician.

1. If treatment for LTBI is not started within two months of the CXR showing no abnormalities indicative of tuberculosis, a repeat CXR should be examined prior to the start of therapy for LTBI to ensure that TB disease has not developed.
2. For clients at high risk of progressing to TB disease (including those < 1 year of age, those co-infected with HIV, or those receiving immunosuppressive therapy), if treatment for LTBI is not started within one month of the CXR showing no abnormalities indicative of tuberculosis, a repeat CXR should be examined before the start of therapy for LTBI to ensure that TB disease has not developed.
3. If the client begins to exhibit symptoms suggestive of TB prior to the start of therapy for LTBI, a repeat CXR should be examined and a physical examination performed to ensure that TB disease has not developed.
4. If client refuses treatment (either initially or during treatment course) for LTBI, educate client on importance of seeking medical evaluation for development of any symptoms suggestive of TB and document refusal in the medical record.

**D. Treatment for TB-infected clients who are contacts to patients with drug-susceptible TB**

1. For **adults**, the following regimens are preferred (**in this order**) by the 2012 Expert Panel:
  - Isoniazid (INH)-Rifapentine (RPT) – see procedure #3: Nursing Management of Clients Treated for LTBI with INH-RPT by DOT Once Weekly for 12 Weeks
  - Rifampin (RIF) for 4 months
  - INH for 9 months
  - INH for 6 months
  - INH/RIF for 3 months – Note: This regimen has been used in the UK and Western Europe for some time and is included as recognition of its status as an available alternative and effective regimen for TB infection. If this regimen is considered for use, consult the authorizing physician and a DSHS-recognized expert TB physician first.
  - For clients that were initially started on treatment for active TB disease, 2 months of standard 4 drug treatment with RIF, INH, pyrazinamide (PZA), and ethambutol (EMB) can be considered adequate treatment for LTBI.

Note: When choosing the best regimen for an individual client, consideration should also be given to the indications/contraindications for each treatment regimen, resources required for DOT (if INH-RPT selected), and likelihood of patient compliance.

2. For **adolescents age 12 years and older**, the preferred regimens are the same as adults, with the following exceptions:
  - When treating with rifampin alone for LTBI, the length of treatment is 6 months for children and adolescents.
  - When treating with INH alone for LTBI, the length of treatment is 9 months for children and adolescents. INH for 6 months should not be recommended.
3. For **children age 2-11 years old**, the preferred regimens are the same as adults, with the following exceptions:
  - When treating with rifampin alone for LTBI, the length of treatment is 6 months for children.
  - When treating with INH alone for LTBI, the length of treatment is 9 months for

children and adolescents. INH for 6 months should not be recommended.

- INH-RPT can be considered on a case-by-case basis when both 1. The circumstances make the completion of 9 months of daily INH unlikely and 2. The likelihood hazard of TB is great (e.g. recent TB infection in a preschool-aged-child). The number of children in this age range who have received INH-RPT is insufficient for assessing tolerability and efficacy. Consult the authorizing physician before using.
4. For **children under the age of 2** the preferred regimens are the same as adults, with the following exceptions:
- When treating with rifampin alone for LTBI, the length of treatment is 6 months for children.
  - INH-RPT was not studied in children < 2 y/o so it is contraindicated in this age group.

**E. Treatment for TB-infected clients who are contacts to INH-resistant, rifampin-susceptible TB**

1. For adults, rifampin for 4 months is recommended.
2. For children and adolescents, when treating with rifampin alone for LTBI, the length of treatment is 6 months.

**F. Treatment for TB-infected clients who are contacts to possible or likely INH- and rifampin-resistant (MDR)-TB and/or XDR-TB** (a rare type of MDR-TB that is resistant to isoniazid and rifampin, plus any fluoroquinolone and at least one of three injectable second-line drugs i.e., amikacin, kanamycin, or capreomycin) **and** who are at high risk for developing TB: consult with a DSHS-recognized expert TB physician for treatment recommendations and appropriate follow-up.

1. All clients with LTBI who are contacts to MDR-TB or XDR-TB, whether on treatment of LTBI or not, need to be followed closely with clinical and radiographic evaluation for 2 years, as specified by the DSHS-recognized expert TB physician.
2. If a TB-infected client is a contact to MDR-TB or XDR-TB and receives treatment for LTBI, DOT shall be provided for the following:
  - Clients <18 years of age.
  - Clients with HIV infection.
  - Clients who are immunocompromised.

**G. Special considerations** for treatment of LTBI apply to the following populations:

1. When INH is chosen for treatment of LTBI in clients with **HIV infection** or those with **radiographic evidence of prior TB**, 9 months rather than 6 months is recommended.
2. Rifampin is generally contraindicated or should be used with caution **in HIV infected clients who are taking protease inhibitors or NNRTIs**.
3. **INH/RPT** is not recommended for the following clients:
  - Children aged <2 years.
  - HIV-infected clients receiving antiretroviral treatment.
  - Pregnant clients or clients expecting to become pregnant during treatment.
  - Clients who have LTBI with presumed INH or RIF resistance.
4. For **pregnant, HIV-negative clients**, INH given daily or twice weekly for 9 or 6 months is recommended.
  - For women at risk of progression of LTBI to disease, especially those who are infected with HIV or who have likely been infected recently, initiation of therapy should not be delayed on the basis of pregnancy alone, even during the first trimester. Consult with the authorizing physician.
  - For women whose risk for active TB is lower, some experts recommend waiting until after delivery to start treatment. Consult with the authorizing physician.

**H. Medication dosages**

Adapted from: <http://www.cdc.gov/tb/publications/LTBI/treatment.htm> (order of drug regimens changed to correspond with preferred regimen order)

Drug(s)	Duration	Dose	Frequency	Total Doses
Isoniazid (INH) and Rifapentine (RPT)	3 months	Adults and Children 12 and over: <b>INH*</b> : 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum <b>RPT*</b> : 10.0–14.0 kg 300 mg 14.1–25.0 kg 450 mg 25.1–32.0 kg 600 mg 32.1–49.9 kg 750 mg ≥50.0 kg 900	Once weekly†	12

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		<i>mg maximum</i>		
Rifampin (RIF)	4 months	Adult: 10 mg/kg*** Maximum dose: 600 mg	Daily	120
Isoniazid (INH)	9 months	Adult: 5 mg/kg Children: 10-20 mg/kg** Maximum dose: 300 mg	Daily	270
		Adult: 15 mg/kg Children: 20-40 mg/kg** Maximum dose: 900 mg	Twice weekly†	76
	6 months	Adult: 5 mg/kg Children: Not recommended Maximum dose: 300 mg	Daily	180
		Adult: 15 mg/kg Children: Not recommended Maximum dose: 900 mg	Twice weekly†	52

†**Intermittent regimens must be provided via directly observed therapy (DOT), i.e., health care worker observes the ingestion of medication.**

\*Isoniazid (INH) is formulated as 100 mg and 300 mg tablets. Rifampentine (RPT) is formulated as 150 mg tablets in blister packs that should be kept sealed until usage.

\*\* The American Academy of Pediatrics recommends an INH dosage of 10-15 mg/kg for the daily regimen and 20-30 mg/kg for the twice weekly regimen.

\*\*\*In the United States, the recommended regimen for treatment of LTBI in children is a 9-month course of INH. For the treatment of LTBI in infants, children, and adolescents when INH could not be tolerated or the child has had contact with a case patient infected with an isoniazid-resistant but rifamycin-susceptible organism the American Academy of Pediatrics recommends 6 months of daily rifampin (RIF) (180 doses) at a dosage of 10-20 mg/kg.

**I. If treatment for LTBI is recommended,**

1. There must be an appropriate **physician order** on record including name of drug(s), dosage, frequency, route and method of administration (directly observed therapy or self-administered therapy), length of treatment, and maximum number of refills:
  - Written order on **TB-400A**, or

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- Written order on a prescription form or physician letterhead, or
  - Verbal order documented in the progress notes.
  - All prescriptions and verbal orders must be followed by form TB-400A with the authorizing physician's signature faxed or mailed within 96 hours.
2. Clients should receive an **initial clinical evaluation and follow-up clinical evaluations** at least monthly with clinical assessment for tuberculosis and disease medication toxicity, in the preferred language of the patient or using an interpreter, recorded on form **TB-205**.
- This evaluation should include questioning about side effects and a brief physical assessment checking for signs of hepatitis.
  - For female clients of childbearing potential: counsel the client that rifamycins may make hormonal contraceptive methods less effective, encourage the client to add a back-up barrier method to prevent pregnancy, and emphasize the importance of avoiding pregnancy while on treatment.
  - Clients should be educated about the symptoms and signs that could be side effects associated with treatment of LTBI and advised to stop treatment and promptly seek medical evaluation when they occur, including: unexplained anorexia, nausea, vomiting, dark urine, icterus, rash, persistent paresthesias of the hands and feet, persistent fatigue, weakness or fever lasting 3 or more days, abdominal tenderness, easy bruising or bleeding, and arthralgia.
  - INH should be withheld if a client's transaminase level exceeds 3 times the upper limit of normal if associated with symptoms and 5 times the upper limit of normal if the patient is asymptomatic. If this occurs with any medication, consult the authorizing physician.
  - Clients should be educated regarding signs and symptoms of tuberculosis. If symptoms of active disease occur, stop the medication(s), complete a medical history (TB-202), obtain a chest x-ray, collect 3 sputum samples, at least two of which are obtained in the early morning on consecutive days, and consult the authorizing physician for medical evaluation. Refer to ATTACHMENT #4: Nursing Management of Clients with or Suspected to have TB Disease (Pulmonary and/or Extrapulmonary Disease).
  - Serious adverse reactions that result in hospitalization or death should be reported to the DSHS TB and Refugee Health Services Branch within two working days on form **EF 12-12274**. Contact the DSHS TB nurse consultant for instructions, if needed. Adverse reactions resulting in hospitalization or death should also be reported to the

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CDC Division of Tuberculosis Elimination at 404-639-8401 or  
LTBI.drug.events@cdc.gov.

- Adverse events or medication errors should be reported to the DSHS TB and Refugee Health Services Branch within five working days on form **EF 12-12274**. Contact the DSHS TB nurse consultant for instructions, if needed. Adverse events should also be reported to FDA MedWatch at <http://www.fda.gov/medwatch>, by submitting a MedWatch Form 3500 (available at [http://www.fda.gov/medwatch/safety/FDA-3500\\_fillable.pdf](http://www.fda.gov/medwatch/safety/FDA-3500_fillable.pdf)) or by calling 1-800-FDA-1088.
3. Clients receiving rifamycins should be counseled about the side effects of rifampin (RIF), rifapentine (RPT), and rifabutin (RBT):
- Hepatotoxicity, evidenced by transient asymptomatic hyperbilirubinemia, may occur in 0.6% of persons taking RIF. Hepatitis is more likely when RIF is combined with INH.
  - Cutaneous reactions, such as pruritus (with or without a rash), may occur in 6% of persons taking RIF. They are generally self-limited and may not be a true hypersensitivity; continued treatment may be possible. Consult the authorizing physician if this occurs.
  - Rarely, rifamycins can be associated with hypersensitivity reactions, including hypotension, nephritis or thrombocytopenia, and manifested by symptoms such as fever, headache, dizziness/lightheadedness, musculoskeletal pain, petechiae, and pruritus.
  - Gastrointestinal symptoms such as nausea, anorexia, and abdominal pain are rarely severe enough to discontinue treatment.
  - Orange discoloration of body fluids is expected and harmless, but patients should be advised beforehand. Soft contact lenses and dentures may be permanently stained.
  - RIF and RPT interact with a number of drugs, causing drug-drug interactions. They are known to reduce concentrations of methadone, warfarin, hormonal contraceptives, and phenytoin. Females using hormonal contraceptives should be advised to consider an alternative method of contraception (e.g., a barrier method).
  - RIF is contraindicated, or should be used with caution, in HIV-infected individuals being treated with certain antiretroviral medications. Substitution of rifabutin for RIF in the 4-month regimen may be considered for such patients. Consult the authorizing physician. RPT should not be used in HIV-infected persons taking antiretroviral therapy.

## J. Directly observed therapy (DOT)

1. Any regimen that is given intermittently (including INH/RPT) should be given only under DOT.
2. Other clients to be considered for DOT, as resources permit:
  - Those with the highest priority for DOT (those at the highest risk of progression from latent to active TB):
    - Clients with HIV infection.
    - Young children who are contacts of infectious patients with pulmonary TB.
  - Household contacts to individuals with active TB and who are receiving DOT.
  - Treatment observed by staff members in certain facilities (such as schools and homeless shelters).
3. For clients receiving DOT, in the event of evacuation, re-establish contact as soon as possible. Confirm location and reinstitute DOT or transfer to new jurisdiction for continuation of treatment.
4. Document doses of medications given by DOT on form **TB-206** (or form **TB-206A** for **INH-RPT** use).

## K. Laboratory testing

1. Baseline laboratory testing and laboratory monitoring during treatment is **not** routinely indicated for all patients at the start of treatment for LTBI.  
**Exceptions:** Clients who should have baseline hepatic measurements of AST, ALT, albumin and bilirubin include those with
  - Initial evaluation suggesting a liver disorder.
  - HIV infection.
  - Current pregnancy or in the immediate postpartum period (within 3 months of delivery).
  - Regular alcohol use.
  - Persons with a history of liver disease.
  - Others at risk for chronic liver disease.
2. Consider testing on an individual basis for older clients or clients who are taking other medications for chronic medical conditions, as ordered by the authorizing physician.
3. If baseline liver function studies exceed the normal range, consult the authorizing physician. Do not give the medication(s) until approved by the treating physician.

4. Active hepatitis and end-stage liver disease are relative contraindications to the use of INH. Consult the authorizing physician if patient has active hepatitis or end-stage liver disease before starting ANY medication.

**5. Routine laboratory monitoring during treatment is indicated for**

- Clients whose baseline liver function tests are abnormal.
  - Other clients at risk for hepatic disease (history of liver disease, HIV infection, HBV, HCV or other chronic hepatitis, sexual or household contact with individuals chronically infected with viral hepatitis, chronic hemodialysis, receipt of clotting factors prior to 1987, pregnant or less than 3 months post-partum, jaundice, substance abuse, taking other potentially hepatotoxic medications, other chronic medical conditions such as DM, CHF, or chronic kidney disease).
6. Laboratory testing may also be indicated for the evaluation of possible adverse effects that occur during the course of treatment, as ordered by the authorizing physician.
    - Obtain liver function studies on the same day, if possible.
    - Do not restart medication without a physician's order.

**L. When INH is used** (including INH-RPT) , **pyridoxine supplementation** should be given to the following:

1. Pregnant clients.
2. Breastfeeding infants - (only if the infant is the one receiving INH).
3. Clients with diets likely to be deficient in pyridoxine.
4. Clients who are at risk for developing paresthesias (such as HIV/AIDS, alcohol use, diabetes mellitus).
5. Clients who experience paresthesias while taking INH.

**Note:** Weekly pyridoxine 50 mg for prophylaxis of isoniazid-associated peripheral neuropathy should be considered with the INH-RPT regimen, especially for persons who are malnourished or predisposed by other illnesses to peripheral neuropathy.

**M. Completion of therapy** is based on total number of doses administered (allowing for minor interruptions in therapy) - not on duration of therapy alone.

1. 9 months of INH = 270 doses, at minimum, (or 193 doses, at minimum, for 5 day/week dosing) administered within 12 months.
2. 6 months of INH = 180 doses, at minimum, (or 129 doses, at minimum, for 5 day/week

dosing) administered within 9 months.

3. 9 months of twice-weekly INH = 76 doses, at minimum, administered within 12 months.
4. 6 months of twice-weekly INH = 52 doses, at minimum, administered within 9 months.
5. 4 months of rifampin (ADULTS) = 120 doses, at minimum, (or 86 doses, at minimum, for 5 day/week dosing) administered within 6 months.
6. 6 months of rifampin = 180 doses, at minimum, (or 129 doses, at minimum for 5day/week dosing) administered within 9 months.
7. INH/RPT = 11 or 12 doses within 16 weeks; doses must be separated by  $\geq 72$  hours to be counted.

#### **N. Interruptions of therapy**

1. When reinstating therapy for clients who have interrupted treatment, obtain a new order from the authorizing physician stating whether to continue the regimen originally prescribed or restart the entire regimen if interruptions were frequent or prolonged enough to preclude completion of treatment as recommended.
2. In either situation, when therapy is restored after an interruption of more than two months, a medical examination and CXR to rule out active TB disease is indicated.

#### **O. Other treatment notes**

1. Refer clients for other medical and social services, as appropriate.
2. If a physician orders to withhold treatment of LTBI, educate clients about TB infection and disease and advise client to seek medical evaluation immediately if any signs or symptoms of TB develop.