Choice of Treatment for Latent TB Infection (LTBI)

Most patients with LTBI should be treated

Persons with risk factors that test positive for LTBI should generally be treated once active TB disease has been ruled out with a CXR, symptom screen, physical exam, and, if indicated, sputum AFB smears, cultures, and nucleic acid amplification testing.

Emphasis on short course treatment of LTBI

Shorter regimens for treating latent TB infection have been shown to be as effective as 9 months of isoniazid, and are more likely to be completed. Use of these shorter regimens is preferred in most patients. Drug-drug interactions and contact to drug resistant TB are typical reasons these regimens cannot be used.

Shorter duration LTBI treatment regimens

Medication	Frequency	Duration
Rifampin	Daily	4 months
Isoniazid + Rifapentine	Weekly	12 weeks*

*11-12 doses in 16 weeks required for completion.

12-dose weekly regimen of INH+rifapentine

- First-line regimen with efficacy equivalent to 9 months of INH.
- Completion rates (85-90%) are much higher than 9 months of INH.
- There is a lower risk of hepatotoxicity than with 9 months of INH.
- Initially studied and recommended using directly observed therapy (DOT), but self-administered therapy found to have equivalent rates of completion in U.S. patients.
- Hypersensitivity syndrome (fevers, flu-like symptoms, presyncope/syncope, hypotension) is observed in some patients. Reactions are typically mild and most patients can continue the regimen.

Rifampin for 4 months

- Preferred treatment in many United States TB clinics.
- Equally effective as isoniazid with higher completion rates.
- Lower risk of hepatotoxicity than with isoniazid
- Potential drug-drug interactions are the major contraindication for use. Check for drug interactions before prescribing.

Isoniazid for 9 months

- Isoniazid for 9 months has low completion rates, often less than 50%.
- Risk of hepatotoxicity is higher with INH than with rifampin or the 12-dose regimen of INH+rifapentine.
- There is a large body of evidence supporting its effectiveness if taken to completion.
- Isoniazid should be used in patients with significant drug-drug interactions with rifamycins.
- Isoniazid should be used with caution in patients with baseline liver disease or who are being administered other hepatotoxic drugs.
- INH can increase the blood level of phenytoin, carbamazepine and some benzodiazepines.
- Refer to product insert or other drug interaction resource for full list of interactions.

Children

Ensuring that children complete treatment is important, particularly those under 5 years who have a high risk for progression to active TB disease because of their young age.

- Clinical trial data supports the use of the INH+ rifapentine regimen in children 2 years and older.
- Clinical trial data supports the use of 4 months of rifampin in children under 18.

Liver Disease

- Rifampin for 4 months or the 12-dose INH+rifapentine regimen have lower risk of hepatotoxicity, thus are preferred for patients with baseline liver disease or hepatotoxicity risk who are not taking medications that have potential drug interactions with rifamycins.
- For those with ALT > 2.5 to 3 times the upper limit of normal, chronic alcohol consumption, or severe liver disease manifested by low albumin and

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Choice of Treatment for Latent TB Infection (LTBI) *—cont.*

coagulopathy or encephalopathy, the risks of LTBI treatment may outweigh benefits. If LTBI treatment is undertaken, close monitoring is indicated.

- When there is an indication for LTBI treatment in patients with advanced liver disease such as future plans for liver transplantation, contact a TB or liver disease expert for LTBI treatment advice.

HIV

- Persons living with HIV are a priority group for LTBI treatment because of elevated risk for progression to TB disease.
- Drug interactions might complicate a rifamycin-containing regimen. Rifabutin in place of rifampin for 4 months is an option to avoid certain interactions.
- Both rifampin and rifabutin interact with the newer tenofovir formulation, tenofovir alafenamide.
- National HIV guidelines recommend INH as the preferred option; rifampin for 4 months and the 12-dose INH+rifapentine regimen as alternatives.
- Treatment should be pursued with consultation with an HIV TB expert.

Immunosuppression (current or planned)

- Significant non-HIV immunosuppression includes organ transplantation, treatment with TNF-alpha antagonist (e.g., infliximab, etanercept, others), steroids (equivalent of prednisone ≥15 mg/day for ≥1 month in adults and ≥2 mg/kg/day for ≥2 weeks in children) or other immunosuppressive medication.
- Immunosuppressed persons are a priority group for LTBI treatment because of higher progression risk to TB disease.
- Drug-drug interactions, particularly with rifamycins, might complicate LTBI treatment and may require additional monitoring.
- For patients with planned immunosuppression, ideally LTBI treatment would be completed prior to immunosuppression. When not possible, at least one month of LTBI treatment should be the goal.

Pregnancy and Breastfeeding

- Pregnancy is not a risk factor for progression to active TB disease.
- Pregnant women with a positive test for LTBI and a risk for rapid progression (e.g., HIV infection, recent exposure and conversion to positive such as in the context of a contact investigation) should be considered for LTBI treatment.
- For women not at risk for rapid progression, LTBI treatment can be delayed until at least 3 months postpartum.
- Both INH and rifampin are considered safe in pregnancy. The INH+rifapentine regimen is under study in pregnancy.
- INH and rifamycins are found in breast milk in small quantities, but are considered safe. There is insufficient data on use of rifapentine in breastfeeding women to recommend use.
- Most experts recommend that exclusively breastfed infants treated with INH should receive pyridoxine supplementation. Pyridoxine supplementation of a breastfed baby whose mother is taking INH is not necessary, but the mother should receive pyridoxine supplementation.

Contact to MDR TB

Treatment of persons with LTBI who are close contacts to a person with infectious MDR TB should be offered treatment for LTBI with a regimen based on the resistance pattern of the index case. Consultation with a clinician with MDR TB expertise is recommended.

Resources

Centers for Disease Control and Prevention, LTBI: Guide for Primary Health Care Providers: cdc.gov/tb/publications/LTBI/treatment.htm

California Department of Public Health Tuberculosis Control Branch (TBCB): cdph.ca.gov/tbcb

California TB Controllers Association: www.ctca.org/

Curry International Tuberculosis Center Consultation Service: currytbcenter.ucsf.edu/ or (877) 390-6682

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