Guidance on Treating Latent TB Infection (LTBI) in Oregon

Introduction: ***Guidance on Treating LTBI in Oregon*** was developed by the TB Program, OHA to assist with decisions related to LTBI treatment. This document does not cover diagnosing LTBI.

The TB Program, OHA can be contacted for clinical consultation at 503-358-8516 or heidi.behm@state.or.us. The Curry International TB Center Warmline is available for clinical consultation at 877-390-6682 (toll-free) or currytbcenter@ucsf.edu.

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Requirements for LPHAs: Treatment of LTBI in Oregon

LPHAs are required to ensure contacts to infectious TB cases and B waiver immigrants with LTBI are treated appropriately for LTBI and treatment is completed.
LPHAs are not required to treat LTBI. Individuals with LTBI may be referred for care.

Overview of Treatment Options for LTBI

Short-course treatment regimens are effective, safe, and have higher completion rates than 6 to 9 months of isoniazid monotherapy (6H/9H). Shorter, rifamycin-based treatment regimens generally have a lower risk of hepatotoxicity than 6H and 9H.

If short-course treatment regimens are not feasible, 6H and 9H are an alternative. Although effective, 6H and 9H have higher toxicity risk and lower treatment completion rates than most short-term treatment regimens.

All treatment must be modified if the patient is a contact to an individual with drug-resistant TB disease. Clinicians should choose the appropriate treatment regimen based on drug susceptibility results of the presumed source case (if known), coexisting medical conditions (e.g., HIV), and potential for drug-drug interactions.

Rifampin (RIF) for 4 months daily (4R) is a preferred regimen for treating LTBI in Oregon. Note RIF interacts with multiple other medications including birth control. Rifampin is covered by most insurance.

Isoniazid (INH) and Rifampin (RIF) (3HR) for 3 months daily is a preferred regimen for treating LTBI in Oregon. Note RIF interacts with multiple other medications including birth control. INH and RIF are covered by most insurance.

Isoniazid (INH) and Rifapentine (3HP) once weekly for 12 doses is safer than INH for 9 months. If given by directly observed therapy (DOT), treatment completion rates are better than INH for 9 months. If the patient self-administers the regimen, treatment rates are “non-superior” to INH for 9 months. In Oregon, decision making about utilizing DOT is up to the provider and patient. Rifapentine interacts with many medications, although to a lesser extent than rifampin. 3HP is not recommended for children < 2 years old. Rifapentine is often in short supply and is not covered by some insurances. Due to the formulation of 3HP the patient will need to take multiple pills at each weekly dose.

INH for 9 months daily (9H) is more effective than INH for 6 months in preventing progression from LTBI to TB disease. A 9 month regimen of INH is recommended; however, a 6 month regimen is acceptable. INH is more likely to cause hepatotoxicity than other regimens.

Initiating treatment of LTBI

Review eligibility for treatment of LTBI

- TB disease has been ruled out.
- Benefits outweigh risks
- No prior completion of TB treatment. Exception may be made for newly exposed immunocompromised contacts.

Obtain pertinent medical history

- Drug susceptibility results of index case (if known).
- Prior side effects with LTBI treatment.
- History of hepatitis or liver disease
- If symptomatic for acute hepatitis (jaundice, abdominal pain/bloating, fatigue) do NOT start treatment. Refer to PCP.
- Active liver disease (e.g. chronic hepatitis B or C; alcoholic liver disease) may be a contraindication to LTBI treatment. Rifampin daily for 4 months is the least hepatoxic regimen:
    - Obtain LFTs.
    - If possible, get records documenting liver disease from PCP.
- Peripheral neuropathy- If patient reports symptoms or prior diagnosis, INH is likely not a good regimen choice.
- Concurrent medications:
    - Assess impact of current medical condition and treatment on LTBI. Rifampin and rifapentine interact with multiple medications including birth control.
- Pregnant or recently postpartum:
    - There is no known adverse effect from LTBI regimens on a developing fetus. However, due to elevated risk of liver toxicity for the patient during pregnancy, defer LTBI treatment until 3 months after pregnancy, unless the patient is a case contact, documented converter, or HIV +.
    - Regularly monitoring LFTs if treating LTBI during pregnancy or postpartum period.
    - Co-manage with prenatal providers.
    - If pregnancy suspected, test for pregnancy.
    - LTBI treatment can be started while breastfeeding. There is no known risk to infant, even if infant is also on LTBI treatment. Some experts recommend starting infant on Vitamin B6 while mother is treated when INH is being used.
- Children
    - Infants and children younger than 5 years old are at high risk for progression to TB disease and invasive disease.
    - Carefully rule out TB disease in children suspected of having LTBI.
    - Dr. Ann Loeffler is the pediatric TB consultant for Oregon. She may be reached through the Curry Center Warmline at**:** 877-390-6682 (toll-free) or currytbcenter@ucsf.edu.

- Excellent resources about treating children with LTBI are available on the Curry Center website: https://www.currytbcenter.ucsf.edu/products/pediatric-tuberculosis-online-presentation/resources

Obtain indicated baseline tests

Baseline liver function testing (AST, ALT, bilirubin) is required for the following patients:

- daily or frequent heavy use of alcohol
- injection drug use in lifetime
- HIV +
- pregnant or postpartum (≤3 months) (if treating for LTBI)
- history of liver disease
- consider for elderly and patients taking other medications

Management of elevated baseline LFTs

- Evaluate risk-benefit of treatment. Also evaluate for underlying liver disease. Shorter course regimens have less risk of hepatotoxicity.
- Advise patients with elevated baseline AST or ALT to abstain from alcohol and recreational drugs and seek substance abuse treatment if indicated.

Notify PCP of initiation of LTBI treatment.

Monthly Monitoring During LTBI Treatment: All Regimens

All patients should be monitored monthly for TB symptoms, side effects and adherence to treatment. The monthly monitoring visit may be done by a RN.

Check for evidence of hepatoxicity, fever, anorexia, dark urine (orange color normal when on RIF/RPT), jaundice, rash, fever or weakness lasting 3 or more days, persistent paresthesia of hands and feet, abdominal tenderness, easy bleeding or bruising, arthralgia, nausea or vomiting.

If a patient has a symptom which the patient or nurse believes may be due to LTBI regimen, treatment should be stopped until the prescribing provider can further assess the adverse effect.

Ongoing Monitoring of Liver Function

Regular (at minimum monthly) monitoring of ALT and AST (transaminase levels) is recommended for the following patients:

- Daily or heavy ETOH use
- Elevated baseline LFTs
- Pregnant or postpartum patients (3 months).
- Chronic liver disease
- Consider in patients > 35 years old if they also have a chronic illness, especially if they take multiple medications

STOP medication if transaminase levels is > 3 times upper limit of normal in presence of symptoms or > 5 times upper limit of normal with no symptoms.

Prescribing LTBI Treatment with Rifampin (RIF) daily for 4 months (4R)

Dose of RIF: See CDC LTBI Treatment Regimens
Special precautions: Possible severe side effects include thrombocytopenia and hepatotoxicity.
Educate patient that RIF will change urine to an orange color and may stain other body fluids orange. RIF interacts with many medications. Do not use if index case is RIF resistant.
Duration of treatment with RIF:
120 doses within 6 months.

Prescribing LTBI Treatment with Isoniazid (INH) and Rifampin (RIF) daily for 3 months (3HR)

Dose of INH and RIF: See CDC LTBI Treatment Regimens
Special precautions: Possible severe side effects include thrombocytopenia and hepatotoxicity.
Educate patient that RIF will change urine to an orange color and may stain other body fluids orange. RIF interacts with many medications. Do not use if index case is RIF resistant.
Duration of treatment with INH and RIF:
90 doses within 6 months

Prescribing LTBI Treatment with 12 weekly doses INH/Rifapentine (3HP)

Dose of INH/Rifapentine See CDC LTBI Treatment Regimens
Special Precautions: Possible severe side effects include thrombocytopenia, hepatotoxicity and hypersensitivity reaction (syncope, hypotension).
Educate patient that Rifapentine will change urine to an orange color and may stain other body fluids orange. Rifapentine interacts with many medications.
25 mg vitamin B6 (pyridoxine) daily is recommended for all patients to prevent peripheral neuropathy from INH.
Do not use if index case is RIF or INH resistant.
Do not use for children < 2 years or for people with HIV/AIDS taking antiretroviral treatment.
Duration of treatment with INH/Rifapentine:
12 doses within 16 weeks. In situations where 12 doses cannot be completed, at least 11 doses can be considered complete. Doses must be given at least 72 hours apart.

Prescribing Treatment LTBI Treatment with Isoniazid (INH)

Dose of Isoniazid (INH) See CDC LTBI Treatment Regimens
Special Precautions: Possible severe side effects include hepatotoxicity. 25 mg

vitamin B6 (pyridoxine) daily is recommended for all patients to prevent peripheral neuropathy.
Do not use if index case is INH resistant.
For children and HIV+, 9 months of INH is advised.
Duration of treatment with INH:
270 doses in 12 months. Although a 9 month regimen is recommended, 6 months of INH is adequate (180 doses in 9 months).

Restarting LTBI Treatment and Changing Regimens

Reassess for symptoms of TB, changes in medical status and contraindications to treatment.
If more than 3 months since last CXR, obtain new CXR before restarting.
Consider restarting regimen from the beginning if patient has missed multiple doses or time since the last dose is longer than two months.
When changing regimens due to adverse effects, it is not always necessary to start the new regimen from the beginning. If more than several doses were taken, it is acceptable to "count" the percentage of the first medication completed and give second medication less that amount (e.g. patient completes 4 doses of 3HP and is switched to 4 months RIF regimen due to intolerable side effects. 4 doses of 3HP=30% treatment completed. Can complete treatment with 84 doses of daily RIF instead of 120 doses).

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