

## Why is Latent TB (LTBI) therapy important?

- LTBI treatment is crucial to eliminate the reservoir of TB and reduce the spread of TB in our community
- In California, an estimated 87% of active TB cases occur from progression of latent infection
  - <https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/TB-Disease-Data.aspx>
- Persons with LTBI have a 10-15% lifetime risk of progressing to active disease.
  - With treatment, the risk reduces by 90% (e.g. 1 – 1.5% life time risk)

## When should LTBI treatment be considered?

Positive Quantiferon or Positive TST

- A **TST 10 mm or greater** is a positive for **any California resident**
- 5mm or greater cutoff : HIV infected persons, contact to TB case (seen by Chest clinic), organ transplant recipients or immunocompromised host, person with fibrotic changes to suggest prior disease

## Latent TB treatment Regimens

**NOTE: TB medications must be dosed at the same time - doses cannot be split at different times**

Treatment Regimen	Dosage	Side Effects	Treatment Considerations
<b>Rifapentine, Isoniazid, Pyridoxine (Vitamin B6) "3HP" Combination</b>  <b>Weekly dosing</b> <b>3-month duration</b>	<u>Adult dosing</u> - INH 900mg <b>weekly</b> - Rifapentine 900mg <b>weekly</b> - Pyridoxine 50mg <b>weekly</b>  <u>Pediatric dosing</u> (Only for age ≥ 2 years) - See table on page 2 for Isoniazid, Rifapentine and B6 dosing	- Nausea, vomiting - Rash - Polyarthralgia - Headache, Dizziness - Hepatotoxicity (0.4%) – increased risk with underlying liver disease - Thrombocytopenia, Neutropenia  Weak inducer of CYP3A4 & P450 2C8/9	Can be administered as self-administered therapy with education on dosing  High Pill burden (Adults 10 tab/dose)  <b>Contraindicated for pregnant or breastfeeding</b> women and drug-interactions with many antiretrovirals
<b>Rifampin "4R" / RIF</b> <b>Daily Dosing</b> <b>4-month duration</b>	<u>Adult dosing</u> 10 mg/kg/day (max 600mg daily)  <u>Pediatric dosing</u> 10-20 mg/kg/day (max 600mg daily)	- Red-orange discoloration of body fluids - Rash, pruritus - Rifamycin hypersensitivity (fever or flu-like symptoms) - Nausea, vomiting - Easy bruising or bleeding - Hepatotoxicity (cholestatic) - Thrombocytopenia , Neutropenia  <b>Strong</b> inducer of CYP3A4 & P450 2C8/9	Significant drug-interactions, <i>Rifabutin 300mg daily</i> can be considered for an alternative as it is a weak inducer; <ul style="list-style-type: none"> <li>- Some medications will still have drug interaction w/ the entire rifamycin class a</li> <li>- Rifabutin has risk of anterior uveitis &amp; greater cytopenia risk</li> </ul>

<b>Isoniazid/Pyridoxine, Rifampin</b> <b>"3HR" Combination</b> <b>Daily Dosing</b> <b>3-month duration</b>	Rifampin, Isoniazid, Pyridoxine <b>daily</b> x 3 months  See Rifampin and Isoniazid section for dosing details	See Rifampin and INH section	Consideration for patients who want to complete LTBI treatment urgently who cannot take rifapentine regimen (3HP)
<b>Isoniazid and Pyridoxine</b> <b>"6H" / INH</b> <b>"9H" / INH</b>  <b>Daily Dosing</b> <b>6-9 month duration</b>	<b>Isoniazid (INH)</b> Adult Dosing: 5mg/kg/daily 300mg daily (max)  Pediatric Dosing: 10 - 15 mg/kg/dose <i>If &gt; 20 kg provide 300mg dosage</i>  <b>Pyridoxine (Vitamin B6, PDX)</b> 1-2 mg/kg/day - Infant 6.25 mg daily - Toddler : 12.5 mg daily - School age, Adolescents and Adults : 25mg daily <i>** Can increase dose to 50mg if neuropathy develops</i>  If has neuropathy comorbidities: 50mg daily	<ul style="list-style-type: none"> <li>- Nausea, vomiting</li> <li>- Rash</li> <li>- Arthralgias</li> <li>- Hepatotoxicity</li> <li>- Peripheral neuropathy</li> <li>- Headaches, dizziness</li> <li>- Fatigue</li> <li>- Lupus like syndrome</li> <li>- Seizures (rare)</li> </ul>	Due to the long duration, higher risk of hepatotoxicity and treatment interruptions, this regimen is not recommended.  It should be reserved for patients with significant rifamycin drug interactions  9-month duration is recommended for patients with high risk of reactivation (e.g. immunocompromised)

**Table 1: Pediatric Isoniazid and Rifapentine dosing for 3HP regimen**

Child's weight	Isoniazid weekly dose	Child's weight	Rifapentine weekly dose
10 – 12 kg	300 mg	10 – 14 kg	300 mg
12.1 – 14 kg	350 mg		
14.1 – 16 kg	400 mg		
16.1 – 18 kg	450 mg		
18.1 – 20 kg	500 mg		
20.1- 22 kg	550 mg		
22.1 – 24 kg	600 mg	25.1–32.0 kg	600 mg
24.1 – 26 kg	650 mg		
26.1– 28 kg	700 mg		
28.1 – 30 kg	750 mg		
30.0 – 32 kg	800 mg		
32.1- 34 kg	850 mg		
Over 34 kg	900 mg maximum dose	≥50.0 kg	900 mg maximum dose

Reference: *Pediatric Tuberculosis: An Online Presentation* by Ann Loeffler, MD. Curry International Tuberculosis Center. Revised 7-26-18

**Pyridoxine (Vitamin B6)**

Adolescents and Adults - 50mg weekly  
 Children: 1-2 mg/kg/dose weekly

**Table 2: Managing Treatment Interruptions**

Treatment Regimen	Goal Doses	Time from start date to complete regimen
3HP (INH, RPT)	11* or 12	16 weeks
4R (RIF)	120	6 months
6H (INH)	180	9 months
9H (INH)	270	12 months
3HR (INH & RIF)	90	4 months

\* If patient completes 11 of 12 doses of 3HP regimen within 16 weeks, then patient is considered to have completed treatment

If patient fails to complete regimen within time specified above, then treatment will need to be restarted.

## Monitoring while on LTBI treatment

- Patients should have **monthly assessments for adherence, symptom reviews and lab monitoring**
- Monthly CBC w/ differential and LFTs are recommended as patients can have asymptomatic drug induced liver-injury
  - If there are limitations to pursuing monthly labs on all patients, a risk assessment should be reviewed prior to starting LTBI treatment.
  - Monthly CBC w/ differential and LFT monitoring is strongly recommended for the following :
    - Patients with underlying liver disease
    - Patients with baseline cytopenias
    - Patients with language barriers or barriers navigating medical system (e.g. New arrivals, Refugees)
- Patients should be instructed on symptoms for hepatitis and advised to stop treatment and seek immediate medical attention if symptoms of hepatitis occur
- TB treatment should be held if the patient is
  - **Symptomatic** and has LFTs at or above 3x upper limit of normal
  - **Asymptomatic** and LFTs are at or above 5x upper limit of normal
- **LTBI treatment monitoring Checklist** has been provided as clinical tool (page 4)
- **If any questions arise regarding treatment concerns or adverse effects please** contact Sacramento County Chest Clinic (916-874-9823) and ask to speak with provider of the day for consultation.

### When to refer to Sacramento County Chest Clinic?

- Patient with an **abnormal CXR**
  - Calcified solitary nodule is not considered abnormal
  - **Do not start LTBI treatment** on these patients
- Patient with **signs of active pulmonary or extrapulmonary disease**
- Pediatrics patients – 5 and below (LTBI or active)
- Contact to active case
- B-1 immigrants and status adjusters (civil surgeon referral)
- Social barriers for adherence – request for direct observed therapy

### **How to refer to Chest Clinic?**

- Fax TB [CMR](#) to 916-854-9614

### **CXR Findings suspicious for Active TB**

- Fibrosis
- Nodule(s) - **Non-calcified**
- Cavitation
- Infiltrates or Consolidation
- Pulmonary lymphadenopathy especially hilar
- Effusion

### **Symptoms concerning for Active TB:**

Patients with any of the following symptoms that *are otherwise unexplained* should be evaluated for active TB disease:

- Cough lasting more than 2-3 weeks
- Fevers, Chills, Night sweats
- Unintended weight loss
- Hemoptysis
- Unexplained fatigue
- Loss of appetite
- Chest pain, dyspnea
- Any extrapulmonary TB symptoms (i.e. lymph node swelling)

**\* Please note, patients can have active Tuberculosis infection and**

- Be asymptomatic
- Can have a negative Quantiferon or TST
- Can have a normal CXR

**If you have any concerns for active TB disease, please refer for further evaluation.**

# LTBI Treatment Monitoring Checklist

**Treatment Start Date** \_\_\_\_\_

**LTBI Regimen (Circle)**

- 3HP (Isoniazid, Rifapentine, B6)      4R (Rifampin)      3HR (Isoniazid, Rifampin, B6)
- 6H (INH, B6)      9H (INH, B6)

Visit Date									
Weight*									

(\*Weight monitoring for pediatric patients or adults w/ low weight who require a dose change)

**Therapy & Adherence Monitoring**

Current dose (mg)											
Refill number											
Takes appropriate number of tablets (Y/N)											
Takes meds at appropriate timing (e.g. weekly or daily) (Y/N)											
Any Missed Doses (Y/N)											

**Adverse Effect Monitoring**

Fatigue?											
Loss of Appetite?											
Rash/Itching?											
Nausea/Vomiting?											
Tingling of fingers or toes?											
Color change: skin/eyes?											
Abdomen tender?											
Headache?											
Pregnant? (Y/N/ N/A)											

If answers yes to any of the following, discuss with provider

**Active TB symptom monitoring (Y/N)**

Cough for greater than 2-3 weeks											
Hemoptysis?											
Adenopathy?											
Fever/chills, night sweats											

If answers yes to any of the following, discuss with provider