**Treatment Regimens for Latent Tuberculosis Infection in Massachusetts**

Massachusetts Department of Public Health

Division of Global Populations and Infectious Disease Prevention



**INTRODUCTION**

Before starting any treatment for latent TB infection, active tuberculosis (TB) disease must be ruled out.

There are three recommended regimens for the treatment of patients diagnosed with latent TB infection. The regimens are summarized in the table below and can be reviewed at <https://www.cdc.gov/tb/topic/treatment/ltbi.htm>.

|  |  |  |  |
| --- | --- | --- | --- |
| **Regimen** | **Duration** | **Interval** | **Administration** |
| Isoniazid +  Rifapentine | 3 months | Once weekly | Oral, directly observed |
| Rifampin | 4 months | Daily | Oral, self-administered |
| Isoniazid | 9 months | Daily | Oral, self-administered |

**Shorter course regimens are preferred because of the higher likelihood of completion of treatment.**

This document provides a brief overview of each treatment regimen for latent TB infection, including for whom the regimen is recommended, dosing, monitoring, and any special considerations. Providers should refer to the product insert for contraindications and side effects.

**ISONIAZID + RIFAPENTINE (3HP or INH+RPT): 3 months (12-dose), once-weekly, directly observed**

**Recommended for**:

Healthy patients aged ≥2 years

The Isoniazid + Rifapentine regimen is ***NOT recommended*** for:

* Children < 2 years of age
* Persons living with HIV infection who are on antiretroviral therapy
* Persons who are presumed to be infected with isoniazid- or rifampin-resistant *M. tuberculosis*
* Women who are pregnant or expect to become pregnant during treatment.

**The Isoniazid + Rifapentine regimen should be considered in persons who are unlikely to complete longer courses of therapy.**

**Dosing**:

Isoniazid:

Adults: 15 mg/kg rounded up to the nearest 50 or 100 mg (900 mg maximum dose)

Children age 2-11 years: 25 mg/kg rounded to the nearest 50 or 100 mg

Rifapentine:

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 kg: 900 mg maximum dose

**Administration**:

Once-weekly oral regimen; MDPH recommends all doses administered under direct observation (DOT) by a trained worker or medical care provider. Pills can be crushed and administered with food.

**Important Side Effects and Adverse Reactions**

Hepatitis (occult or symptomatic), thrombocytopenia, nausea, vomiting, rash, flu-like syndrome, light-headedness, headache, hypotension, syncope, and drug interactions (see below).

**Monitoring**

Direct observation of treatment administration by a healthcare worker: Because missed doses, altered dosing intervals, or amounts of drug taken could jeopardize efficacy or safety, the Isoniazid + Rifapentine regimen should be administered by DOT. The DOT can be done at the provider’s office or at a location chosen for mutual convenience (*e.g.,* home or school clinic).

* + *At each DOT encounter*, patients should be questioned, in detail, about possible side effects and instructed to seek immediate medical attention if they have symptoms consistent with drug toxicity, such as fevers, yellow eyes/skin, abdominal pain, syncope, or rash.
  + In addition, if any of the above symptoms, was noted following the previous dose, the subsequent dose of Isoniazid + Rifapentine should be held pending clinical evaluation. Unexplained syncope is an important, although rare, complication of this regimen; it usually is preceded by prodromal symptoms (nausea, dizziness, weakness, near-syncope, headache) following the dose. Subsequent doses should be held pending evaluation, if a person responds affirmatively to pre-dose questioning for any of these symptoms.

Patients should undergo a clinical assessment *by a health care provider* *at least monthly*. The assessment should include inquiries about side effects and a physical examination.

Blood tests (CBC/platelets and hepatic enzymes) are recom­mended at baseline for patients with HIV infection, history of liver disease or regular alcohol use, and persons >35 years of age. The clinician may also elect to obtain baseline studies for their other patients. Repeat (or follow-up) measurements should be done if:

* + The baseline result is abnormal
  + Patient has symptoms due to adverse reactions.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Week | | | | | | | | | | | |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| Medical evaluation/ monitoring | x |  |  |  | x |  |  |  | x |  |  |  |
| DOT | x | x | x | x | x | x | x | x | x | x | x | x |

**Special precautions**

*Rifapentine, like rifampin, affects the metabolism of many drugs*, such as hormonal contraceptives, antidepressants, oral anticonvulsants, antihypertensives, antiarrhythmic drugs, oral anticoagulants, methadone, and others. Appropriate adjustments must be made, if treatment with Rifapentine is being considered.

Patients over the age of 35 years are at increased risk of hepatoxicity.

**RIFAMPIN (RIF): 4 months, daily, self-administered**

**Recommended for**:

Persons who reliably can take self-administered, daily therapy and have no contraindications to taking Rifampin or any rifamycin medication. May be used in pregnant women and in children.

**Dosing**:

Adults: 10mg/kg/d weight-based; maximum 600mg/day

Children <12 years: 10-20 mg/kg/d weight-based; maximum 600mg/day

**Administration**:

Once daily, self-administered.

**Important Side Effects and Adverse Reactions**

Hepatitis (occult or symptomatic), thrombocytopenia, nausea, vomiting, rash, discoloration of body fluids (including tears, with possible staining of soft contact lenses), drug interactions (see below).

**Monitoring**:

Patients must understand adherence and safety issues. Patients should be instructed to hold treatment and to contact their medical provider if adverse effects are suspected.

Patients should undergo a *clinical assessment* *at least* monthly by a health care provider, including inquiries about side effects and a physical examination.

Blood tests (CBC/platelets and hepatic enzymes) are recom­mended at baseline for patients with HIV infection, history of liver disease, regular alcohol use, or pregnancy. The clinician may also elect to obtain baseline studies for their other patients. Repeat (or follow-up) measurements should be done if:

* + The baseline result is abnormal
  + Patient is pregnant or in the immediate postpartum period, or at high risk of adverse reactions
  + Patient has symptoms of adverse reactions

**Special precautions**:

*Rifampin affects the metabolism of many drugs*, such as hormonal contraceptives, antidepressants, oral anticonvulsants, antiarrhythmic drugs, antihypertensives, oral anticoagulants, methadone, and others. Appropriate adjustments must be made if treatment with rifampin is being considered.

Orange discoloration of body fluids, including urine, is expected and harmless, but patients should be advised beforehand. Soft contact lenses and dentures may be permanently stained.

**ISONIAZID (INH): 9 months, daily, self-administered**

**Recommended for**:

Adults and children with latent TB infection who reliably can take self-administered, daily therapy, and have no contraindication to taking isoniazid.

**Dosing**:

Adults: 5 mg/kg/d weight-based; typical (maximum) dose is 300 mg/day

Children: 10-20 mg/kg/d weight-based; maximum dose is 300 mg/day

Isoniazid is also available in 50 mg/5 ml in 70% sorbitol syrup. Because sorbitol may cause diarrhea, crushed pills in a small quantity of food may be preferred, when possible.

Pyridoxine (vitamin B6), 10-25 mg/d, may prevent peripheral neuropathy and central nervous system effects; it usually is administered with INH in children and in persons who are nutritionally deficient.

**Administration**:

Once daily, self-administered

**Important Side Effects and Adverse Reactions**

Hepatitis (occult or symptomatic), thrombocytopenia, nausea, vomiting, rash, hair loss, drug interactions (see below).

**Monitoring**:

Patients must understand adherence and safety issues and will know to hold treatment and contact their provider if adverse effects are suspected.

Patients should undergo a *clinical assessment at least monthly by a health care provider*, including inquiries about side effects and a physical examination.

Blood tests (CBC and hepatic enzymes) generally are not recom­mended. For patients with HIV infection, history of liver disease, regular alcohol use, pregnancy (or 3-4 months postpartum), or age >35 years, blood tests should be performed at baseline. Repeat (or follow-up) measurements should be done if:

* + The baseline result is abnormal
  + Patient is pregnant or in the immediate postpartum period, or at high risk of adverse reactions
  + Patient has symptoms of adverse reactions.

**Special precautions**: Isoniazid interacts with other drugs including seizure medications (e.g., carbamazepine, valproic acid, phenytoin), azole-class drugs used to treat fungal infections, theophylline.

Persons taking acetaminophen or consuming alcohol are at increased risk of hepatotoxicity, as are persons over the age of 35 years and pregnant or recently postpartum women (especially Black or Hispanic women).

**RESOURCE INFORMATION**

Centers for Disease Control and Prevention. Recommendations for use of an isoniazid-rifapentine regimen with direct observation to treat latent *Mycobacterium tuberculosis* infection. MMWR 2011;60(48) p1650-1653. <http://www.cdc.gov/mmwr/pdf/wk/mm6048.pdf>

Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000;49(No. RR-6) <http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf>

Centers for Disease Control and Prevention, Division of Tuberculosis Elimination

# Latent Tuberculosis Infection: A Guide for Primary Health Care Providers; Treatment of Latent TB Infection. <https://www.cdc.gov/tb/publications/ltbi/treatment.htm>

Treatment regimens for latent TB infection. <https://www.cdc.gov/tb/topic/treatment/ltbi.htm>

Global TB Institute. Diagnosis and treatment of latent tuberculosis infection. 2015. <http://globaltb.njms.rutgers.edu/educationalmaterials/productfolder/ltbidrugcard.php>

Massachusetts Department of Public Health[**TB Information for Your Patients**](https://www.mass.gov/lists/tb-information-for-your-patients-in-english-and-other-languages)<https://www.mass.gov/lists/tb-information-for-your-patients-in-english-and-other-languages>

For further information, contact the MDPH Tuberculosis Program at 617-983-6970.

**REGULATIONS**

**105 CMR 300**

Reportable diseases, surveillance, and isolation and quarantine requirements

<https://www.mass.gov/regulations/105-CMR-30000-reportable-diseases-surveillance-and-isolation-and-quarantine>