

## LTBI Videos-Monitoring Patients on Treatment for LTBI

This program is presented by the Global Tuberculosis Institute and is based on recommendations from the Centers for Disease Control and Prevention. This is the fourth and final video in a series for primary care providers. In this video, you'll learn about monitoring patients on treatment for latent TB infection, also called LTBI or TB infection. We'll discuss potential adverse effects of medications for LTBI, monitoring patients on treatment, and assessing and addressing adherence to treatment. Other videos discuss screening for, diagnosing, and treating LTBI.

Treatment of LTBI prevents development of TB disease on an individual level and is an important component of TB prevention efforts. Treatment is safe and effective, and serious adverse drug reactions are rare. However, as we'll discuss, there are potential adverse effects from the medications and periodic monitoring is recommended to evaluate for adherence to treatment, signs and symptoms of TB disease, and adverse drug reactions.

As with any treatment, you must weigh the risks and benefits for each individual patient. Visit the CDC website and call your local health department if you have any questions about adverse effects and drug interactions.

### Adverse Effects

Many providers are aware of the risk for hepatotoxicity with the medications used to treat LTBI, however, the risk is minimal in most patients and should not deter treatment. Certain patients are at higher risk for hepatotoxicity. This can be considered both in regimen selection and in the monitoring plan.

When starting patients on treatment for LTBI, describe expected side effects and potential adverse effects of the medications *and* instruct your patients about what to do if they experience adverse reactions. Tell patients to contact you if they notice any other unusual new symptoms or have any symptoms they are concerned about. Be sure to emphasize that most adverse reactions are minor and *can* be treated.

### *Isoniazid*

Possible adverse effects of isoniazid, often referred to as I-N-H, include hepatic enzyme elevation, rash, gastrointestinal symptoms, mild CNS effects, and peripheral neuropathy. Asymptomatic elevation of serum liver enzyme concentrations occurs in 10 to 20 percent of people, and usually returns to normal when treatment is discontinued. In most people with mild asymptomatic elevation of LFTs, the elevation is transient and resolves even if isoniazid is maintained. It's generally recommended to withhold I-N-H if transaminase levels reach or exceed 3 times the upper limit of normal with symptoms, and 5 times the upper limit among people with no symptoms. We'll talk more about this in the section on laboratory monitoring.

Clinical or symptomatic hepatitis, with nausea, vomiting, or right upper quadrant pain occurs in less than 1 percent of people taking I-N-H. Risk factors include alcohol use, liver disease, or the risk of liver disease, and use of other medications that are metabolized by the liver.

Approximately one percent of people taking isoniazid develop peripheral neuropathy, which is more likely to occur in those with HIV infection, diabetes, alcoholism, malnutrition, pregnancy, or other conditions associated with neuropathy. Individuals with these conditions should receive pyridoxine supplementation to prevent neuropathy. Those on the 12-dose once weekly isoniazid and rifapentine regimen should receive 50 milligrams of vitamin B6 per week. Those on other I-N-H containing regimens should receive 25-50 milligrams per day.

### *Rifamycins*

Rifampin and rifapentine can also have hepatotoxic effects. A very small percentage of patients may experience hepatotoxicity. People taking rifampin or rifapentine may also experience gastrointestinal symptoms, such as nausea, anorexia, and abdominal pain. However, these symptoms are not usually severe enough to stop treatment. Some people taking these medications may also experience cutaneous reactions, such as pruritus.

Tell patients taking rifampin or rifapentine they will notice a normal orange discoloration of bodily fluids, including urine and tears. Contact lenses may be permanently stained.

Get a list of all other medications your patient is taking, including over the counter medications. Rifampin and rifapentine can interact with many other drugs and may be contraindicated in patients on certain HIV antiretrovirals. Visit this website for current guidelines and information on drug-drug interactions with HIV antiretrovirals, as guidelines are updated frequently. If you are unfamiliar with these medications, consultation with an expert is recommended.

Rifamycins are known to reduce concentrations of the medications listed on your screen, including methadone, hormonal contraceptives, and anticoagulants. Patients on these medications require close monitoring and dose adjustments of the companion medication may be necessary. Instruct women to use a barrier method of birth control while they are taking either rifampin or rifapentine, because hormonal contraceptives may not be as effective.

In addition to the potential adverse reactions associated with the individual medications, systemic drug reactions, or hypersensitivity, can occur in rare cases in patients on the 12-dose once weekly isoniazid and rifapentine regimen. In most circumstances, this is mild and does not result in discontinuation of treatment. S-D-Rs may include flu-like symptoms such as fever, headache, dizziness, and myalgias, as well as pruritis. Keep vigilant for more severe systemic drug reactions, such as hypotension and thrombocytopenia.

If adverse drug reactions occur in persons on *any* regimen, a prompt clinical evaluation should be conducted, with treatment changes as indicated. For most regimens, adverse reactions can be monitored and managed and treatment can be completed. For the 12-dose once weekly isoniazid and rifapentine regimen, conservative management, and continuation of treatment under observation can be considered in the presence of mild to moderate adverse drug reactions. In case of possible severe adverse reactions in patients on *any* regimen, discontinue treatment and provide supportive medical care.

Report any adverse events to the CDC Division of Tuberculosis Elimination by email to this address and to FDA MedWatch at this website.

#### Monitoring:

Periodic monitoring is important to ensure safe and effective treatment for LTBI. Be sure to establish a plan for monitoring when you start treatment. To assess the patient's progress, conduct clinical monitoring, order appropriate lab tests, and provide relevant education.

#### *Clinical monitoring*

Monitor patients at least monthly to assess progress. Evaluate for adherence to treatment, signs and symptoms of TB disease, and any adverse reactions, such as signs and symptoms of hepatitis, which are listed on your screen.

#### *Laboratory monitoring*

Although baseline liver function tests are not routinely indicated, some patients do need baseline measurements of serum A-S-T, A-L-T, and bilirubin. Baseline testing can be considered on an individual basis, and should be obtained for people with HIV, those with a history of liver disease, regular alcohol use, risk factors for liver disease including use of other hepatotoxic medications, and women who are pregnant or post-partum.

Periodic retesting is recommended for people with initial abnormal results and for those who are at risk of liver disease. Additional lab tests should be ordered if a patient develops any symptoms of hepatitis. For patients whose treatment is discontinued due to elevated transaminases, laboratory monitoring of transaminases should be continued until they have returned to normal. For those on I-N-H containing regimens, consider completion of treatment with 4 months of daily rifampin, after transaminases have returned to normal, depending on the patient's risk of progressing to TB disease and willingness to complete treatment.

Other laboratory tests may be indicated for patients with underlying medical conditions.

#### Assessing and addressing adherence

Assess patient adherence during monthly monitoring visits since treatment for LTBI is *only* effective if patients complete their treatment regimen. Remember, use of rifamycin-based short course regimens increases treatment completion.

Many factors can affect a patient's adherence and a patient-centered approach, including ongoing education, can help to identify and address any challenges or barriers. Monitoring visits provide an opportunity to reinforce educational messages, including reminders about the importance of treatment adherence.

Emphasize possible side effects and adverse reactions. Provide patients with written instructions for adverse effects and contact information for your office, so they can inform you if these occur.

Be sure patients understand the signs and symptoms of serious adverse reactions, such as hepatitis, and tell patients to stop treatment and promptly seek medical attention if any potentially serious adverse reactions occur. Provide information at a language level the patient can understand and use interpreters or a language line if needed. See the resource link at the end of this video for access to patient education materials.

Use open-ended questions to identify any concerns or challenges your patient may be having with treatment. Potential barriers for treatment completion could include side effects from treatment, not understanding the regimen, perhaps due to language, or financial concerns such as copays for clinical visits and medications. Patients may also have difficulty with transportation to get to their appointments, or to get medication refills. Work to address any barriers and help your patient complete treatment.

Strategies may include ongoing education, suggestions for medication administration to minimize side effects, medications to alleviate them, or changing treatment regimens. Your local health department *may* be able to assist with free or low-cost medicines, directly observed therapy, and case management for individuals with an increased risk of progression to TB disease.

#### *Conclusion*

Remember, it is important to consider potential adverse effects of medications, monitor patients on treatment, including monthly clinical monitoring, and laboratory monitoring for certain patients, and assess and address adherence, including educating patients, and identifying and addressing barriers. This approach will help patients successfully complete treatment for LTBI, which prevents development of TB disease.

Thank you for viewing this video on monitoring patients on treatment for LTBI, which is the fourth and final video in a series. The other videos discuss screening, diagnosis, and treatment. For more information and the additional resources mentioned in this video, visit this website: [globaltb.njms.rutgers.edu/](http://globaltb.njms.rutgers.edu/)