

III. Treatment of Latent Tuberculosis Infection

A. Overview

Latent tuberculosis infection (LTBI) is defined as infection with *Mycobacterium tuberculosis* in the absence of signs and symptoms without any other clinical evidence of active tuberculosis disease. Identifying people with LTBI affords an opportunity to prevent future progression to active tuberculosis disease, thereby reducing future illness and interrupting the cycle of transmission. Unfortunately, the tests used to diagnose LTBI are imperfect and rely on the host immune response to the bacterium to detect infection. As a result, they are not optimally sensitive for LTBI, particularly in hosts with compromised immune systems such as young children, people with the human immunodeficiency virus, and people taking immunosuppressive drugs. Furthermore, they cannot discriminate between LTBI and active TB disease, so further evaluation is required to make that determination. Finally, they do not reliably respond to LTBI treatment, so cannot be used to determine whether LTBI treatment was successful (i.e. all the tuberculosis bacteria were cleared from the patient's body).

From a public health perspective, the key elements of a successful LTBI treatment program are as follows:

- Targeted at people with significant risk for infection. Testing people who are at low risk of infection is a poor use of resources and will produce many false-positive tests, resulting in unnecessary exposure to medications that may cause harm without benefit.
- Tailored to patient populations of local interest. LTBI testing and treatment programs that do not facilitate testing, initiation, and completion of treatment by taking logistical, financial, and cultural needs of local populations will not be effective.
- Safe for the wide variety of patients encountered in clinical practice. **Most patients with LTBI will never develop active TB even if they do not take LTBI treatment.** LTBI treatment, by definition, involves exposing people who are not sick to medications that have potential to make them sick. The risks of LTBI treatment must be minimized by using the safest possible regimens in the safest possible systems, with redundant measures to detect adverse medication events promptly and minimize harm.

B. Priorities for LTBI treatment

Not all people with a positive test for LTBI require LTBI treatment. As a rule of thumb:

- People at highest or high priority for LTBI treatment should always be offered LTBI treatment, and aggressive attempts at education should be provided to persuade them to take it
- People at medium priority for LTBI treatment should always be offered LTBI treatment
- People at low or lowest priority for LTBI treatment should only be offered LTBI treatment after discussion and counseling with a healthcare provider. Such discussion and counseling should include the following steps:
 - Offering a second test for LTBI in people with no epidemiologic risk for TB exposure (see chapter II for more information)

- Review of the patient's risk of progression to active TB using the website www.tstin3d.com
- Review of the risks of LTBI treatment:
 - Interaction with other medications
 - Approximately 2-5% risk of stopping therapy due to a medication-associated adverse event (side effect)
 - Approximately 0.3-0.4% risk of liver toxicity due to medication (assuming 3 months of isoniazid-rifapentine or 4 months of rifampin are used), or 1-3% risk of liver toxicity if 6-9 months of isoniazid is used

People who meet any of the following criteria are at high risk to progress to active TB, and should be given the highest priority for LTBI treatment regardless of initial TST or IGRA results:

- HIV-seropositive or other severely immunocompromised individuals who are recent contacts to known or suspected infectious TB disease, regardless of previous LTBI treatment
- HIV-seropositive with fibrotic changes on chest radiograph consistent with prior TB who have received inadequate or no prior treatment for TB disease
- Children under 5 years of age identified as recent contacts to known or suspected infectious TB disease

People who have a TST reaction ≥ 5 mm or a positive IGRA and meet any of the following criteria are at relatively high risk to progress to active TB, and should be given high priority for LTBI treatment:

- HIV-seropositive
- Contact to known or suspected infectious TB disease within the past two years
- Fibrotic changes on chest radiograph consistent with prior TB disease who have received no or inadequate prior treatment for active TB
- Immunocompromised individuals, e.g., receiving ≥ 15 mg per day of Prednisone for 1 mo., other immunosuppressive drugs, organ transplant, or people taking or considering taking tumor necrosis factor (TNF) inhibitors like etanercept (Embrel®), infliximab (Remicade®) or anakinra (Kineret™) or adalimumab (Humira®)

People who have a TST reaction ≥ 10 mm or a positive IGRA and meet any of the following criteria are at moderately high risk to progress to active TB, and should be given medium priority for LTBI treatment:

- Foreign-born individuals from Asia, Africa, Caribbean, Latin America, Mexico, South America, Pacific Islands or Eastern Europe
Low prevalence countries are USA, Canada, Japan, Australia, Western Europe, and New Zealand
- Those who have converted their TST within two years
- Those with medical conditions which place them at high risk for TB disease
 - Diabetes mellitus
 - Chronic renal failure
 - Chronic malabsorption syndrome
 - Leukemia, lymphomas, Hodgkin's disease
 - Cancer of the head or neck
 - Silicosis

- Weight loss of $\geq 10\%$ ideal body weight
- Gastrectomy or intestinal bypass
- Injection drug or crack cocaine user
- Children < 4 years of age
- Children and adolescents exposed to high risk adults
- People residing for > 1 month in a high incidence area
- Mycobacteriology lab personnel
- Residents of homeless shelters
- Prison inmates and personnel
- Jail personnel
- Healthcare personnel

People who have a TST reaction ≥ 10 mm or a positive IGRA and meet any of the following criteria are either at relatively low risk for TB infection or present logistical challenges to LTBI treatment that often outweigh the benefits of attempting treatment, and should be given low priority for LTBI treatment:

- Residents of long-term care facilities
- Jail inmates
- Personnel at homeless shelters
- Personnel at adult day care centers for people living with HIV

People who have a TST reaction ≥ 15 mm or a positive IGRA and have no risk factors for TB exposure are at low risk for both TB infection and progression to active TB. Such people should be given lowest priority for LTBI treatment.

C. Standards for Managing Latent TB Infection

1. Prior to initiating any treatment for LTBI, review all medications the individual is taking and assess for potential drug interactions with TB medications.
2. Decisions to treat LTBI should take into consideration the individual's risk for developing tuberculosis disease compared with the risk of adverse reactions to TB medication (see counseling discussion in part B above).
3. All people with LTBI should be offered HIV testing, regardless of perceived risk for HIV infection.
 - A chest X-ray to exclude active tuberculosis disease is required before starting any treatment for latent infection:
 - A chest X-ray taken within the past three months is required for asymptomatic new converters, HIV+ individuals, and those who are severely immunocompromised.
 - People who are not new converters or immunocompromised, have a history of a prior positive TST/IGRA with a normal chest radiograph within the past two years, are asymptomatic, and wish to start LTBI treatment do not require a new chest radiograph prior to starting LTBI treatment
 - A posterior-anterior (PA) view chest X-ray should be obtained on all adults:
 - With a newly identified positive TST or IGRA

- With symptoms suggestive of TB disease regardless of TST/IGRA results.
 - With negative TST/IGRA and starting treatment for LTBI due to medical risk (e.g. close contacts with HIV infection).
 - A PA and lateral view chest X-ray should be obtained on children under 5 years of age:
 - With a newly identified positive TST/IGRA.
 - With symptoms suggestive of TB disease regardless of TST/IGRA
 - Who are close contacts to an infectious TB case
 - Pregnant women should have a PA view chest X-ray with appropriate shielding as soon as possible, even during the first trimester of pregnancy due to the risk of progressive and/or congenital TB.
 - Individuals with a previously documented positive TST/IGRA and a negative chest X-ray who do not wish to take LTBI treatment or who have previously completed LTBI treatment should have a repeat X-ray only when symptoms or tuberculosis disease are present. For screening purposes, a Record of TB Screening DHHS 3405 can be used.
4. If the patient reports a cough and sputum results are pending, wait until a final negative sputum culture report is issued before starting medications.
 5. Obtain a medical history including a review of symptoms and previous adverse reactions to TB drugs (e.g., drug fever, rash), underlying liver disease and INH-associated liver injury and offer HIV testing (**see TB Epidemiological Record – DHHS 1030**).
 6. For self-administration, never give more than a 30-day supply of TB medication.
 7. The health care provider or an interpreter should be conversant in the patient’s own language to ensure good communication.
 8. All patients should be instructed to stop LTBI medication and seek immediate medical consultation if they experience symptoms that may suggest a severe medication side effect. These symptoms may include, but are not limited to, loss of appetite, abdominal pain, nausea, vomiting, jaundice, abnormal bruising or bleeding, abnormally low blood pressure, or fainting.
 9. All patients must be clinically assessed at least monthly for adverse reactions and the findings documented (see TB Flow Sheet – DHHS 2810).
 10. The appropriate drug information fact sheet(s) should be reviewed with the patient.
 11. Health department TB nurses may manage latent TB infection under standing orders signed by a physician or contract TB clinician. We have included sample standing orders for each regimen at the end of this chapter. Your TB clinician must choose the regimen that is to be used and if the drug that you have a standing order for is not appropriate for a patient you must get a specific order for that patient. Standing orders should not be used for treating patients that have a low risk for progression to TB disease. Low risk patients must be evaluated by a health care provider to determine if the low risk individual is a good candidate for treatment.

12. When a patient is treated for active tuberculosis with rifampin, isoniazid, pyrazinamide, and ethambutol for eight weeks and active tuberculosis is ruled out, the patient can be considered adequately treated for latent TB infection

D. Standard Regimens for Adults ≥ 12 Years

1. Isoniazid plus rifapentine for 12 weeks

- Isoniazid plus rifapentine, administered once weekly for 12 weeks, is a preferred option for treatment of latent TB infection.
- Isoniazid is administered once weekly at the same time as rifapentine, dosed according to the table below (Chapter III, section I).
- This regimen is contraindicated for pregnant and breastfeeding women.
- Missed doses may be administered within 72 hours of the intended dose
- Rifapentine interacts with many other drugs. **The patient's medication regimen should be completely reviewed for potential interactions prior to prescribing rifapentine.** Please see Chapter VII of the NC TB Control Manual for links to resources regarding potential drug interactions.
- With approval of the local TB clinician, self-administered isoniazid and rifapentine is acceptable. Directly observed preventive therapy should be reserved for people at high risk for progression to TB disease and who are less likely to complete self-administered therapy.
- Note that 11 doses taken within 16 weeks is adequate for completion of INH/rifapentine treatment

2. Rifampin for four months

- This regimen is a preferred option for treatment of latent TB infection, especially in the following circumstances:
 - Intolerance or allergy to isoniazid;
 - Individual is a close contact to isoniazid-resistant, rifampin-susceptible TB;
- Rifampin interacts with many other medications, including oral contraceptives and warfarin. **The patient's medication regimen should be carefully examined for potential medication interactions before prescribing rifampin.**
- Rifampin dosage is in the table below (Chapter III, section I).
- Daily rifampin (120 doses) should be given for a total of four months within a six-month period
- **Rifampin by itself may not be given on a twice-weekly schedule.**

3. Isoniazid plus rifampin for three months

- This regimen is a preferred option for treatment of latent TB infection, particularly if rifapentine is not available but the patient is otherwise a good candidate for isoniazid/rifapentine
- Rifampin interacts with many other medications, including oral contraceptives and warfarin. **The patient's medication regimen should be carefully examined for potential medication interactions before prescribing rifampin.**
- Isoniazid and rifampin dosages are in the table below (Chapter III, section I).

4. Isoniazid for six to nine months
 - Six months of isoniazid should be offered to patients with intolerance to rifampin/rifapentine or unacceptable drug interactions with rifampin/rifapentine who are otherwise candidates for treatment of latent TB infection
 - Nine months of isoniazid is preferred for people living with HIV or other severe immunocompromising conditions
 - Dosage for isoniazid is in the table below (Chapter III, section I). 18 daily doses or 52 twice-weekly doses should be ingested within a nine-month period of time if a six-month course is intended; 270 daily doses or 78 twice-weekly doses should be ingested within a 12-month period of time if a nine-month course is intended. Twice-weekly doses of isoniazid should be separated by a minimum of 72 hours.
 - Isoniazid for LTBI is relatively contraindicated for individuals with active hepatitis or end-stage liver disease and should not be used in these individuals without a specific physician order.
5. Isoniazid and rifapentine for one month
 - Isoniazid and rifapentine for one month have been studied as LTBI treatment among people age 13 and older living with HIV who were either at high risk for LTBI infection or had a positive TST/IGRA
 - This regimen may be considered, in consultation with the NC TB Medical Director, for use in circumstances in which a high-risk patient is deemed unlikely to complete a longer regimen

E. Standard Regimens for Infants and Children (< 12 Years)

Since all TB medications are dosed based on weight and weight can change relatively rapidly in growing children, children should be weighed monthly while on LTBI treatment and medication doses adjusted accordingly.

1. Isoniazid plus rifapentine for 12 weeks
 - This regimen is a preferred option for latent TB treatment in children over two years of age.
 - This regimen cannot be used in children less than 2.
 - Directly observed preventive therapy is preferred for children (but often a parent may observe therapy)
 - Isoniazid is administered at the same time as rifapentine at the doses described in the table below (Chapter III, Section I).
 - Missed doses can still be administered up to 72 hours before the next dose.
 - Rifapentine interacts with many other drugs. **The patient's medication regimen should be completely reviewed for potential interactions prior to prescribing rifapentine.** Please see Chapter VI of the NC TB Control Manual for a *partial* list of drugs that interact with rifapentine.
 - 11 doses taken within 16 weeks is adequate for completion of INH/Rifapentine treatment.

2. Four months of rifampin
 - This regimen is a preferred option for latent TB treatment in children, especially in the following circumstances
 - Intolerance to isoniazid;
 - Individual is a close contact to isoniazid-resistant, rifampin-susceptible TB
 - Children under 2 years of age
 - Dosage for rifampin is in the table below (Chapter III, section I). 120 daily doses should be ingested within a six-month period.
 - **Rifampin by itself may not be given on a twice-weekly schedule.**
 - Rifampin interacts with many other medications, including oral contraceptives and warfarin. The patient's medication regimen should be carefully examined for potential medication interactions before prescribing RIF.
 - Children weighing more than 40 kg should be dosed as an adult

3. Isoniazid plus rifampin for three months
 - This regimen is a preferred option for treatment of latent TB infection, particularly if rifapentine is not available or the child is under two years age but the patient is otherwise a good candidate for isoniazid/rifapentine
 - Rifampin interacts with many other medications, including oral contraceptives and warfarin. **The patient's medication regimen should be carefully examined for potential medication interactions before prescribing rifampin.**
 - Isoniazid and rifampin dosages are in the table below (Chapter III, section I).

4. Isoniazid for six to nine months
 - Six months of isoniazid should be offered to patients with intolerance to rifampin/rifapentine or unacceptable drug interactions with rifampin/rifapentine who are otherwise candidates for treatment of latent TB infection
 - Nine months of isoniazid is preferred for people living with HIV or other severe immunocompromising conditions
 - Dosage for isoniazid is in the table below (Chapter III, section I). 180 daily doses or 52 twice-weekly doses should be ingested within a nine-month period of time if a six-month course is intended; 270 daily doses or 78 twice-weekly doses should be ingested within a 12-month period of time if a nine-month course is intended. Twice-weekly doses of isoniazid should be separated by a minimum of 72 hours.
 - Isoniazid for LTBI is relatively contraindicated for individuals with active hepatitis or end-stage liver disease and should not be used in these individuals without a specific physician order.

F. **LTBI in Pregnant Women**

1. Chest X-rays
 - Due to the risk of progressive and/or congenital TB, pregnant women should have a PA view of the chest (with appropriate shielding) as soon as possible, even during the first trimester of pregnancy, if they have a positive TST or IGRA.

2. Asymptomatic TST/IGRA-positive pregnant women with a negative chest X-ray should start latent tuberculosis treatment as soon as possible if they have one of the following factors:
 - HIV infection;
 - Close contact to infectious TB disease;
 - TST/IGRA conversion; or
 - Medical condition associated with high risk of progression to active TB disease.

3. Asymptomatic TST/IGRA positive pregnant women with a negative chest X-ray and no risk factors may elect to delay preventive therapy until after delivery, but it is acceptable to offer preventive therapy with isoniazid or rifampin during pregnancy with appropriate monitoring. Recent data suggested that isoniazid preventive therapy during pregnancy among HIV-seropositive mothers was associated with somewhat worse pregnancy outcomes (Gupta A et al., New England Journal of Medicine 2019; 381: 1333); whether a similar effect would be observed in HIV-seronegative people or with rifampin is unknown.

4. Treatment Regimens
 - a. Rifampin for four months
 - Rifampin for four months is a preferred regimen for treatment of latent TB in pregnant women, particularly in the following circumstances:
 - Individual is a close contact to isoniazid-resistant, rifampin-susceptible TB;
 - Individual is high-risk for progression to active TB but is unlikely to adhere to a full nine-month course of isoniazid; and
 - Individual is at relatively high risk for hepatotoxicity from isoniazid (e.g. excess alcohol use, concurrent hepatotoxic medication).
 - Rifampin interacts with many other medications, including oral contraceptives and warfarin. **The patient's medication regimen should be carefully examined for potential medication interactions before prescribing rifampin.**
 - Daily rifampin (120 doses) should be given for a total of four months within a six-month period.
 - **Rifampin by itself may not be given on a twice-weekly schedule.**

 - b. Isoniazid for six to nine months:
 - Isoniazid for six months is an acceptable regimen for pregnant women who cannot take rifampin due to intolerance or drug interactions
 - Nine months of isoniazid is preferred for people living with HIV or other severe immunocompromising conditions
 - Dosage for isoniazid is in the table below (Chapter III, section I). 180 daily doses or 52 twice-weekly doses should be ingested within a nine-month period of time if a six-month course is intended; 270 daily doses or 78 twice-weekly doses should be ingested within a 12-month period of time if a nine-

month course is intended. Twice-weekly doses of isoniazid should be separated by a minimum of 72 hours.

- Isoniazid for LTBI is relatively contraindicated for individuals with active hepatitis or end-stage liver disease.

5. The small concentration of TB medication in breast milk does not produce toxicity in the newborn; therefore, breast-feeding should not be discouraged.

G. Pyridoxine

1. Peripheral neuropathy is associated with the use of isoniazid but is uncommon at doses of 5 mg/kg of body weight.

2. Pyridoxine (B₆) 25 mg. daily or 50 mg. twice weekly (once weekly with INH/rifapentine) should be given on the same schedule with isoniazid if any of the following risk factors for peripheral neuropathy are present:

- a. Diabetes mellitus;
- b. Average alcohol use of > three drinks per day or binge drinking (\geq five drinks in one day intermittently);
- c. Malnutrition;
- d. HIV infection;
- e. Pregnancy, if prenatal vitamin does not contain at least 25 mg of B₆; and
- f. Seizure disorder.

3. Individuals who develop peripheral neuropathy while taking daily B₆ should have their B₆ dose doubled. If neuropathy is not resolved in two weeks, consult physician.

4. Individuals on dialysis should be given B₆ 50mg on the same schedule with isoniazid.

5. Pyridoxine (B₆) is recommended for exclusively breastfed infants and for children and adolescents on meat and milk deficient diets; children with nutritional deficiencies, including all symptomatic HIV-infected children.

a. Dosage for infants and children (contact physician for order):

1 mg/kg body weight daily (maximum 25mg daily); dose can be rounded up as needed. For example, a 14 lb. infant weighs 6.36 kg and therefore would receive 6.36 mg of pyridoxine. Using a graduated syringe or dropper, 6.4 mg would be acceptable.

b. Preparation:

Pharmacist should prepare 99 cc of simple sugar syrup and add one vial (100 mg) of injectable pyridoxine. This preparation results in a concentration of 1mg of pyridoxine per cc of syrup.

c. Administration:

By mouth, using a pediatric oral syringe or dropper; the syringe or dropper should be graduated in 0.1 - 0.2 cc to allow for correct dosing.

e. Storage:

- Syrup should be placed in an amber glass bottle and stored in the refrigerator. The syrup is stable for 30 days.
- f. Alternatively, pyridoxine tablets (25 mg) may be quartered (6.25 mg), crushed, and mixed with baby food or breast milk for administration.

H. Drug Chart for Treating LTBI

Drug Dosages for Treating LTBI		
Regimen	Dosage (maximum dose is listed in parenthesis)	
	Adults (age >12)	Children (age 12 and under) *
Rifampin 4 months daily	10 mg/kg (600 mg)	15-20 mg/kg (600 mg)
Isoniazid/rifapentine 12 weeks once weekly*	15 mg/kg (900 mg)	25 mg/kg (900 mg)
Isoniazid	Weight	Dose
Rifapentine	Child weight	Dose
	10.0-14 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
Isoniazid 6-9 months daily**	5 mg/kg (300 mg)	10-20 mg/kg (300 mg)
Isoniazid 6-9 months twice weekly**	15 mg/kg (900 mg)	20-40 mg/kg (900 mg)
Isoniazid plus rifampin 3 months daily		
Isoniazid	5 mg/kg (300 mg)	10-20 mg/kg (300 mg)
Rifampin	10 mg/kg (600 mg)	15-20 mg/kg (600 mg)
Isoniazid/rifapentine 1 month daily*	5 mg/kg (300 mg)	N/A
Isoniazid	Weight	Dose
Rifapentine	< 35 kg	300 mg
	35-45 kg	450 mg
	>45 kg	600 mg

* Children weighing 40 kg or more should be dosed as adults

** Pyridoxine 25 mg (daily) or 50 mg (once/twice weekly) should be administered to patients at risk of peripheral neuropathy on these treatment regimens

I. Monitoring of LTBI treatment

While LTBI treatment is reasonably safe and well-tolerated, side effects may occur and in rare cases, may be serious. A brief overview of common/important drug side effects is contained in the table below.

Drug(s)	Side effect	Symptoms/signs
Isoniazid, rifampin, rifapentine	Hepatotoxicity	Nausea, vomiting, fatigue, dark urine, yellow eyes
Isoniazid	Peripheral neuropathy	Numbness, tingling, burning, especially in the toes and fingers
Isoniazid, rifampin, rifapentine	Hypersensitivity	Rash, fever
Rifampin, rifapentine	Thrombocytopenia	Easy bruising/bleeding, petechial skin rash
Rifampin, rifapentine	Flu-like syndrome	Myalgias, fever
Rifampin	Interstitial nephritis	Fatigue, bloody urine, decreased urine output
Isoniazid, rifapentine	Hypotension	Dizziness, presyncope, syncope

1. Isoniazid monitoring

- a. Prior to initiating isoniazid, obtain a baseline hepatic function panel¹ (includes: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and total bilirubin) on the following individuals:
 - Average alcohol use of \geq three drinks per day or binge drinking (\geq five drinks in one day, intermittently) (one drink is defined as one 12 oz beer, 4 oz of wine or 1 oz of liquor).
 - HIV-positive.
 - Underlying liver disease.
 - Pregnant women.
 - Women up to three months postpartum.
 - Those currently taking other potentially hepatotoxic drugs such as:¹
 - ◆ "statin" drugs;
 - atorvastatin (Lipitor)
 - lovastatin (Mevacor)
 - pravastatin (Pravachol)
 - rosuvastatin (Crestor)
 - simvastatin (Zocor)
 - ◆ anticonvulsant drugs;
 - carbamazepine (Tegretol)

¹ Note that this is an incomplete list of drugs with potential for hepatotoxicity

- phenytoin (Dilantin)
- valproic acid (Depakote)
- ◆ methotrexate; and
- ◆ miscellaneous antidiabetic agents for Type 2 diabetes.
 - pioglitazone (Actos)
 - rosiglitazone (Avandia)

If baseline lab tests are abnormal consult the physician before initiating treatment for LTBI.

- b. Obtain hepatic function panel² monthly on the following individuals who are taking isoniazid:
- Baseline hepatic function panel results are abnormal;
 - Pregnant women;
 - Women up to three months postpartum the immediate postpartum period (i.e., within three months of delivery);
 - Those with symptoms of adverse reactions;
 - Taking potentially hepatotoxic drugs (above list);
 - Those with chronic active hepatitis B or those with hepatitis C;
 - Chronic or binge use of alcohol; and
 - Those with HIV infection.

Hold therapy if signs or symptoms of hepatotoxicity are present, draw hepatic function panel and consult physician with results.

- c. See the last pages of this chapter for a flowchart on how to address hepatotoxicity in patients taking TB medications.
- d. If a patient has an adverse reaction to the treatment for LTBI that results in the patient being hospitalized or dies this must be reported to the CDC National Surveillance for Severe Reactions (NSSAE) by sending an e-mail to them at LTBIdrugevents@cdc.gov saying you have a patient that died or required hospitalization as a result of being treated for LTBI. They will contact the sender of the e-mail and will get further information.

2. Rifampin monitoring

- a. Prior to initiating rifampin, obtain a baseline CBC with platelets, and hepatic function panel¹ on the following individuals:

² Hepatic Function Panel includes: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and total bilirubin.

- average alcohol use of \geq three drinks per day or binge drinking (\geq five drinks in one day, intermittently) (one drink is defined as one 12 oz beer, 4 oz of wine or 1 oz of liquor).
 - HIV positive.
 - Underlying liver disease.
 - Pregnant women.
 - Those currently taking other potentially hepatotoxic drugs such as:³
 - ◆ "statin" drugs;
 - atorvastatin (Lipitor)
 - lovastatin (Mevacor)
 - pravastatin (Pravachol)
 - rosuvastatin (Crestor)
 - simvastatin (Zocor)
 - ◆ anticonvulsant drugs;
 - carbamazepine (Tegretol)
 - phenytoin (Dilantin)
 - valproic acid (Depakote)
 - ◆ methotrexate; and
 - ◆ miscellaneous antidiabetic agents for Type 2 diabetes.
 - pioglitazone (Actos)
 - rosiglitazone (Avandia)
- b. If baseline CBC with platelets and liver function panel are outside normal limits, consult physician before initiating treatment for LTBI.
- c. Obtain hepatic function panel⁴ monthly on the following individuals who are taking rifampin:
- Baseline hepatic function panel results are abnormal;
 - Pregnant women;
 - Women up to three months postpartum the immediate postpartum period (i.e., within three months of delivery);
 - People with symptoms of adverse reactions;
 - People taking potentially hepatotoxic drugs (above list);
 - People with chronic active hepatitis B or those with hepatitis C;
 - Chronic or binge use of alcohol; and
 - People living with HIV infection.

Hold therapy if signs or symptoms of hepatotoxicity are present; draw hepatic function panel and consult physician. RIF can also cause immunologic reactions, including fevers, anemia, and thrombocytopenia. Hold therapy for any new fevers or easy bruising/bleeding.

3. Isoniazid/rifapentine monitoring

³ Note that this is an incomplete list of medications with potential for hepatotoxicity

⁴ Hepatic Function Panel includes the following: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and total bilirubin.

- a. Prior to initiating isoniazid/rifapentine, obtain a baseline hepatic function panel¹ (includes: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and total bilirubin) and complete blood count (CBC) with platelets on the following individuals:
- Average alcohol use of \geq three drinks per day or binge drinking (\geq five drinks in one day, intermittently) (one drink is defined as one 12 oz beer, 4 oz of wine or 1 oz of liquor).
 - HIV-positive.
 - Underlying liver disease.
 - Women up to three months postpartum.
 - People currently taking other potentially hepatotoxic drugs such as:⁵
 - ◆ "statin" drugs;
 - atorvastatin (Lipitor)
 - lovastatin (Mevacor)
 - pravastatin (Pravachol)
 - rosuvastatin (Crestor)
 - simvastatin (Zocor)
 - ◆ anticonvulsant drugs;
 - carbamazepine (Tegretol)
 - phenytoin (Dilantin)
 - valproic acid (Depakote)
 - ◆ methotrexate; and
 - ◆ miscellaneous antidiabetic agents for Type 2 diabetes.
 - pioglitazone (Actos)
 - rosiglitazone (Avandia)

If baseline lab tests are abnormal consult the physician before initiating treatment for LTBI.

- b. Individuals on iso should be monitored clinically at least once per month while on medications. At each visit, patients should be questioned and examined for the following:
- Signs or symptoms of hepatotoxicity (e.g., anorexia, nausea, vomiting, abdominal pain, jaundice);
 - Signs or symptoms of hypersensitivity (fever, chills, myalgias; and)
 - Signs or symptoms of thrombocytopenia (easy bruising or bleeding, petechiae, purpura).
 - Signs or symptoms of low blood pressure (dizziness, fainting)

Hold therapy if signs or symptoms of hepatotoxicity, hypersensitivity, and/or thrombocytopenia are present.

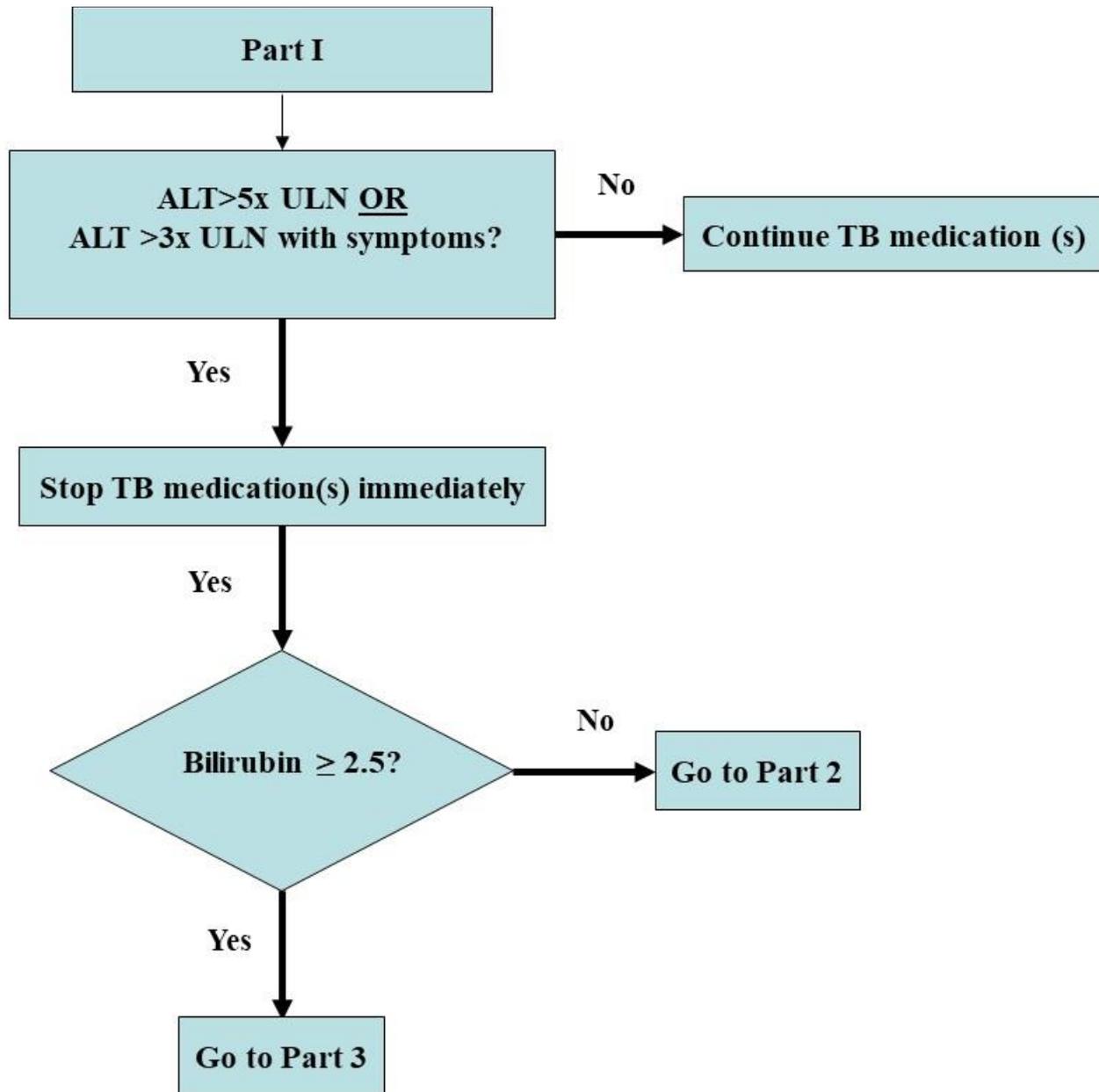
- c. Obtain hepatic function panel⁶ monthly on the following individuals who are taking isoniazid/rifapentine:

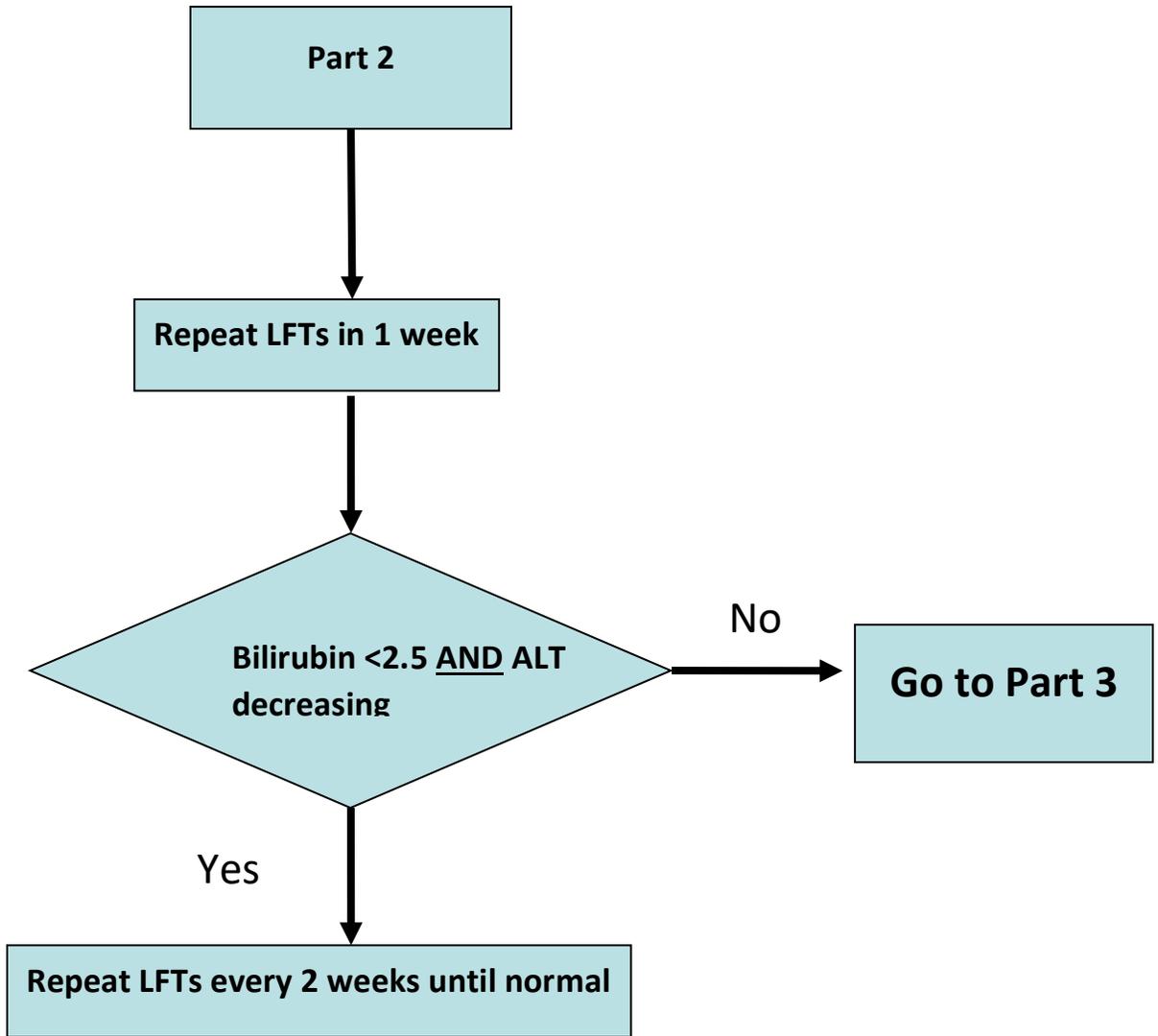
⁵ Note that this is an incomplete list of drugs with potential for hepatotoxicity

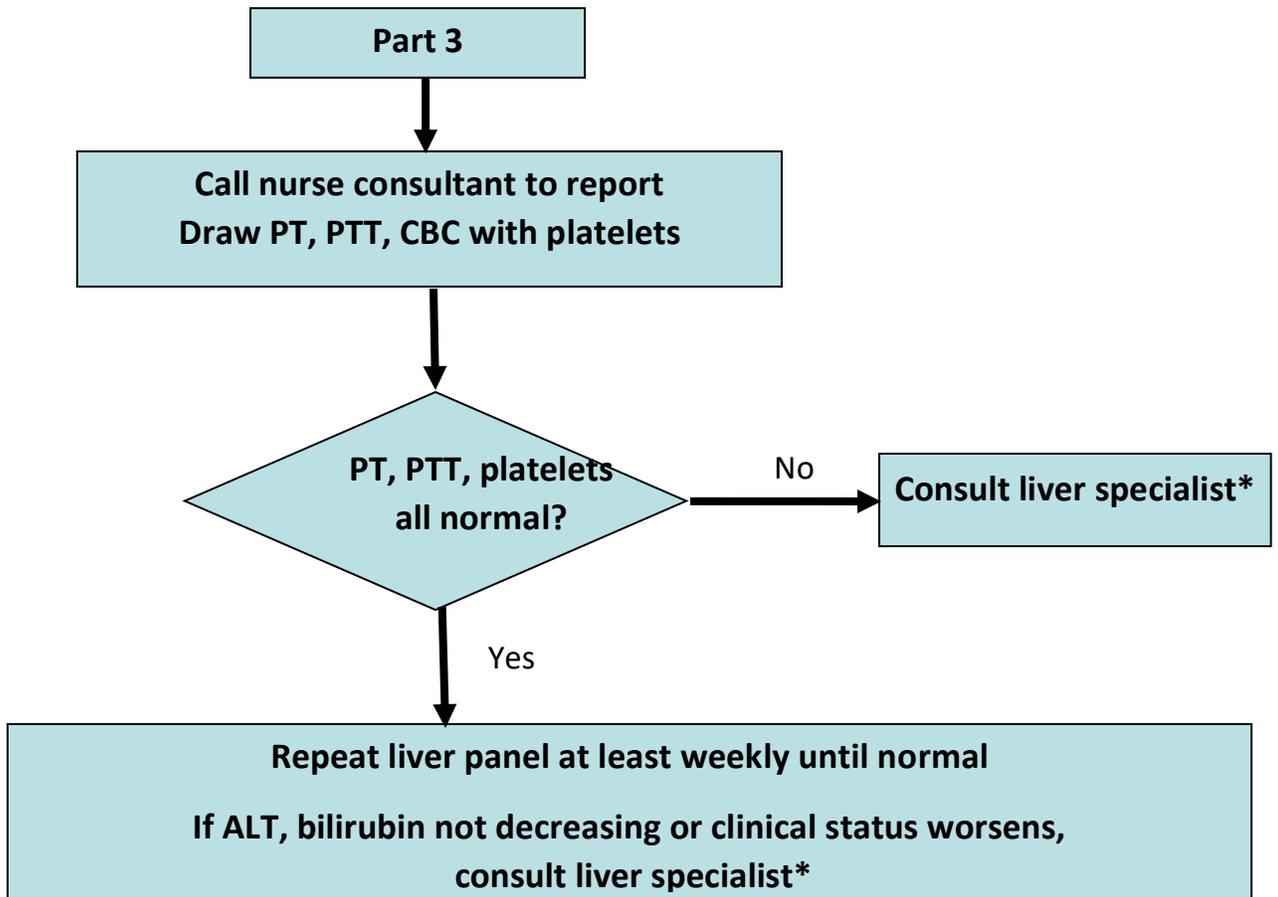
⁶ Hepatic Function Panel includes: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and total bilirubin.

- Baseline hepatic function panel results are abnormal;
 - Pregnant women;
 - Women up to 3 months postpartum the immediate postpartum period (i.e., within 3 months of delivery);
 - Those with symptoms of adverse reactions;
 - People taking potentially hepatotoxic drugs (above list);
 - People with chronic active hepatitis B or those with hepatitis C;
 - Chronic or binge use of alcohol; and
 - People living with HIV infection.
- d. See the last few pages of this chapter for a flowchart on how to address hepatotoxicity in patients taking TB medications.
- e. If a patient has an adverse reaction to the treatment for LTBI that results in the patient being hospitalized or dies this must be reported to the CDC National Surveillance for Severe Reactions (NSSAE) by sending an e-mail to them at LTBIdrugs@cdc.gov saying you have a patient that died or required hospitalization as a result of being treated for LTBI. They will contact the sender of the e-mail and will get further information.

J. Hepatotoxicity Flowchart







* The nurse consultant/state TB medical consultant can facilitate this referral—please contact immediately

K. Standing Orders

Health Departments can use standing orders for the treatment of LTBI. They must be in the NC Board of Nursing format and must be signed by a physician annually. Below are sample standing orders of all the LTBI treatment regimens. You may only have one regimen using standing orders. If that regimen cannot be used, you must contact the physician for an alternative regimen.

Sample Standing Order: Evaluation and Treatment of Latent Tuberculosis (TB) Infection Using Rifapentine and Isoniazid

Assessment: All PHNs employed or contracted by the agency who have completed a TB program orientation will use the following standing orders for the evaluation and treatment of latent TB infection using rifapentine and isoniazid if the patient denies a-j under the subjective findings and a-f under the objective findings and g-j of the objective findings are present.

Subjective findings:

Patient denies the following:

- a. Productive cough, fever, night sweats, weight loss, loss of appetite, shortness of breath, chest pain, and unexplained fatigue;
- b. Completing treatment of latent tuberculosis infection (a minimum of 6 months of isoniazid or 4 months of rifampin or a minimum of 11 doses of isoniazid with rifapentine).
- c. History of hepatitis or liver disease.
- d. History of adverse reaction to rifampin, rifapentine or isoniazid.
- e. Heavy alcohol use in the last 12 months (Heavy is defined as \geq 5 drinks per day for men and 4 for women on \geq 5 days/month. 1 drink = 12 oz beer = 4 oz wine = 1 shot liquor)
- f. Being pregnant or up to 3 months postpartum.
- g. Being exposed to a drug resistant case of TB.
- h. Being on potentially hepatotoxic drugs.
- i. Taking medication that may interact with rifampin, rifapentine or isoniazid.
- j. Having nausea, vomiting, loss of appetite, dark urine, jaundice, malaise, abdominal discomfort, skin rash, fever, or unexplained bruising/bleeding.

Objective findings:

- a. The chest X-ray is not suggestive of previous TB.
- b. The individual is not HIV positive
- c. Is not on hemodialysis.
- d. Is not taking methotrexate.
- e. Is not a child less than 2 years old.
- f. The baseline or follow-up lab work is not abnormal.
- g. Is \geq 2 years old but less than 5 years old and a contact to an infectious TB case and treatment needs to be started in the window period between the initial negative TST and the repeat 8 weeks later. **OR**
- h. The TST reaction is \geq 5 mm or has a positive IGRA and meets any of the following criteria:
 - Contact to known or suspected infectious TB disease within the past two years
 - Fibrotic changes on chest radiograph consistent with prior TB disease who have received no or inadequate prior treatment for active TB
 - Immunocompromised individuals, e.g., receiving \geq 15 mg per day of Prednisone for 1 mo., other immunosuppressive drugs, organ transplant, or

people taking or considering taking tumor necrosis factor (TNF) inhibitors like etanercept (Embrel®), infliximab (Remicade®) or anakinra (Kineret™) or adalimumab (Humira®) **OR**

- The TST reaction is ≥ 10 mm or has a positive IGRA and meets any of the following criteria:
 - Foreign-born individuals from Asia, Africa, Caribbean, Latin America, Mexico, South America, Pacific Islands or Eastern Europe
 - Low prevalence countries are USA, Canada, Japan, Australia, Western Europe, and New Zealand*
 - Those who have converted their TST within two years
 - Those with medical conditions which place them at high risk for TB disease
 - Diabetes mellitus
 - Chronic renal failure
 - Chronic malabsorption syndrome
 - Leukemia, lymphomas, Hodgkin's disease
 - Cancer of the head or neck
 - Silicosis
 - Weight loss of $\geq 10\%$ ideal body weight
 - Gastrectomy or intestinal bypass
 - Injection drug or crack cocaine user
 - Children < 4 years of age
 - Children and adolescents exposed to high risk adults
 - People residing for > 1 month in a high incidence area
 - Mycobacteriology lab personnel
 - Residents of homeless shelters
 - Prison inmates and personnel
 - Jail personnel
 - Healthcare personnel
- i. No acid-fast bacterium (AFB) culture pending or all AFB cultures are reported as negative for *Mycobacterium tuberculosis* (*M. tuberculosis*).
- j. Chest X-ray interpretation indicating no evidence of active TB disease.

Plan of Care:

1. Implementation:

- a. If the patient has anything listed under subjective a-j or objective a-f or has a positive TST or IGRA but has no risk factors for progression to TB, do not engage the standing order and consult with the physician for specific orders.
- b. Obtain posterior-anterior (PA) view chest X-ray, additionally
 - I. Use appropriate shielding for pregnant women,
 - II. If a patient had a previously documented positive TST/IGRA at any time in the past and a negative PA chest X-ray within the last two years, the chest X-ray does not need to be repeated if the patient reports no symptoms of active TB.

- III. A chest X-ray taken within the past three months is required for asymptomatic new converters, HIV positive individuals, and those who are taking medication that cause immunosuppression.
- IV. Children under age five should also have a lateral view chest X-ray.
- c. Complete Tuberculosis Epidemiological Record (DHHS 1030).
- d. Obtain HIV test unless the patient specifically refuses or has documentation of testing with the past 6 months.
- e. For HIV negative adults (greater than 12 years of age) Isoniazid is administered at a dose of 15 mg/kg (maximum 900 mg), plus rifapentine using the following dosage chart:
- | | |
|----------------|-------------------------|
| 10 – 14 kg | 300 mg |
| 14.1- 25.0 kg | 450 mg |
| 25.1 -32.0 kg | 600 mg |
| 32.1 - 49.9 kg | 750 mg |
| > 50.0 kg | 900 mg (Maximum dosage) |
- given together once weekly for 12 weeks, taken within a 16-week period. Missed doses can still be administered up to 72 hours before the next dose.
- f. For HIV negative children (ages 2-12, inclusive): initiate isoniazid 25 mg/kg (maximum 900 mg), plus rifapentine using the following dosage chart:
- | | |
|----------------|-------------------------|
| 10 – 14 kg | 300 mg |
| 14.1- 25.0 kg | 450 mg |
| 25.1 -32.0 kg | 600 mg |
| 32.1 - 49.9 kg | 750 mg |
| > 50.0 kg | 900 mg (Maximum dosage) |
- given together once weekly for 12 weeks, taken within a 16-week period. Missed doses can still be administered up to 72 hours before the next dose.
- g. Initiate pyridoxine (B6) 50 mg weekly if the patient is an adult and has any of the following conditions:
- Diabetes
 - Alcohol use of > 3 drinks per day
 - Malnutrition
 - Seizure disorder
- h. Review all medications the patient is currently taking with a doctor, pharmacist or a drug-drug interaction product to determine if there are any contraindications to coadministration of isoniazid or rifapentine with the patient's current medications.
- i. If the patient is on a medication that will interact with rifampin or rifapentine, is allergic or intolerant of rifampin or rifapentine, or is a contact to a rifampin resistant case of tuberculosis, consult with physician for treatment orders.
- j. If the patient is on a medication that will adversely interact with isoniazid, is allergic to or intolerant of isoniazid, or is a contact to an isoniazid resistant case of tuberculosis, consult with physician for treatment orders.
- k. **Hold therapy if signs or symptoms of hepatotoxicity are present (nausea, vomiting, loss of appetite, dark urine, jaundice, malaise, and abdominal discomfort), draw hepatic function panel and consult physician.**
- l. **Hold therapy if there are signs and symptoms of immunologic reactions such as fever, easy bleeding or bruising, or low hemoglobin (< 13.5 for men, < 12.5 for women, and < 11 for children (between 2 years and 12 years). Draw CBC with platelets and consult physician.**

Nursing Action:

- a. Advise the patient of common adverse reactions to rifapentine and isoniazid.
- b. Advise the patient to hold medications and contact the health department if adverse reactions such as nausea, vomiting, loss of appetite, dark urine, jaundice, malaise, abdominal discomfort, skin rash, fever, easy bleeding or bruising, or low hemoglobin (< 13.5 for men, < 12.5 for women, and < 11 for children (between 2 years and 12 years) occur.
- c. Ensure that physician reviews laboratory results and documents this per the agency policy on reviewing laboratory results. (Agency should list the name of this policy here)

Criteria for calling the Physician:

- a. If the patient develops side effects from the medications such as, nausea, vomiting, loss of appetite, dark urine, jaundice, malaise, abdominal discomfort, skin rash, fever, easy bleeding or bruising, or low hemoglobin (< 13.5 for men, < 12.5 for women, and < 11 for children (between 2 years and 12 years) occur.
- b. If the patient becomes pregnant.
- c. If the hepatic function or CBC with platelets laboratory results are outside the normal limits.
- d. If there is any question about whether to implement the standing order.

Follow-up Requirements:

- a. Evaluate the patient monthly by completing the Tuberculosis Flow Sheet (DHHS 2810).
- b. Recalculate medication dosage monthly after weighing

Resources: NC TB Control Program Policy Manual 2018 edition.

Legal Authority: Nurse Practice Act, G.S. 90-171.20 (7) (f) & (8) (c)

Date written: _____

Approved by: _____

Date: _____

Approved by: _____

Date: _____

Approved by: _____

Date: _____

Sample Standing Order: Evaluation and Treatment of Latent Tuberculosis (TB) Infection Using Rifampin

Assessment: All RNs employed or contracted by the agency who have completed a TB program orientation will initiate the following standing orders for the evaluation and treatment of latent TB infection using rifampin (RIF) if the patient denies a-j under the subjective findings and a-e under the objective findings and f-i of the objective findings are present.

Subjective findings:

Patient denies the following:

- a. Productive cough, fever, night sweats, weight loss, loss of appetite, shortness of breath, chest pain, and unexplained fatigue;
- b. Completed treatment of latent tuberculosis infection (a minimum of 6 months of isoniazid or 4 months of rifampin or a minimum of 11 doses of isoniazid with rifapentine).
- c. History of hepatitis or liver disease.
- d. History of adverse reaction to rifampin.
- e. Excess/binge alcohol use (Average alcohol use of \geq three drinks per day or binge drinking (\geq five drinks in one day, sporadically) (one drink is defined as one 12 oz beer, 4 oz of wine or 1 oz of liquor).
- f. Being pregnant or up to 3 months postpartum.
- g. Being exposed to a drug resistant case of TB.
- h. Being on potentially hepatotoxic drugs.
- i. Taking medication that may interact with rifampin.
- j. Having nausea, vomiting, loss of appetite, dark urine, jaundice, malaise, abdominal discomfort, skin rash, fever, or unexplained bruising/bleeding.

Objective findings:

- a. The chest X-ray is not suggestive of previous TB.
- b. The individual is not HIV positive
- c. Is not on hemodialysis.
- d. Is not taking methotrexate.
- e. The baseline or follow-up lab work is not abnormal.
- f. Is \geq 2 years old but less than 5 years old and a contact to an infectious TB case and treatment needs to be started in the window period between the initial negative TST and the repeat 8 weeks later. **OR**
- g. The TST reaction is \geq 5 mm or has a positive IGRA and meets any of the following criteria:
 - Contact to known or suspected infectious TB disease within the past two years
 - Fibrotic changes on chest radiograph consistent with prior TB disease who have received no or inadequate prior treatment for active TB
 - Immunocompromised individuals, e.g., receiving \geq 15 mg per day of Prednisone for 1 mo., other immunosuppressive drugs, organ transplant, or people taking or considering taking tumor necrosis factor (TNF) inhibitors like etanercept (Embrel®), infliximab (Remicade®) or anakinra (Kineret™) or adalimumab (Humira®) **OR**

The TST reaction is ≥ 10 mm or has a positive IGRA and meets any of the following criteria:

- Foreign-born individuals from Asia, Africa, Caribbean, Latin America, Mexico, South America, Pacific Islands or Eastern Europe
Low prevalence countries are USA, Canada, Japan, Australia, Western Europe, and New Zealand
 - Those who have converted their TST within two years
 - Those with medical conditions which place them at high risk for TB disease
 - Diabetes mellitus
 - Chronic renal failure
 - Chronic malabsorption syndrome
 - Leukemia, lymphomas, Hodgkin's disease
 - Cancer of the head or neck
 - Silicosis
 - Weight loss of $\geq 10\%$ ideal body weight
 - Gastrectomy or intestinal bypass
 - Injection drug or crack cocaine user
 - Children < 4 years of age
 - Children and adolescents exposed to high risk adults
 - People residing for > 1 month in a high incidence area
 - Mycobacteriology lab personnel
 - Residents of homeless shelters
 - Prison inmates and personnel
 - Jail personnel
 - Healthcare personnel
- h. No acid fast bacterium (AFB) culture pending or all AFB cultures are reported as negative for Mycobacterium tuberculosis (M.tb).
- i. Chest X-ray interpretation indicating no evidence of active TB disease. .

Plan of Care:

1. Implementation:

- a. If the patient has anything listed under the subjective a-j or the objective findings a-e or has a positive TST or IGRA but has no risk factors for progression to TB do not engage the standing order and consult with the physician for specific orders.
- b. Obtain posterior-anterior (PA) view chest X-ray, additionally:
 - I. Use appropriate shielding for pregnant women,
 - II. If a patient had a previously documented positive TST/IGRA at any time in the past and a negative PA chest X-ray within the last two years, the chest X-ray does not need to be repeated if the patient reports no symptoms of active TB.
 - III. A chest X-ray taken within the past three months is required for asymptomatic new converters, HIV positive individuals, and those who are taking medication that cause immunosuppression.
 - IV. Children under age five should also have a lateral view chest X-ray.
- c. Complete Tuberculosis Epidemiological Record (DHHS 1030).

- d. Obtain HIV test unless the patient specifically refuses or has documentation of testing with the past 6 months.
- e. For adults (greater than 12 years of age) over 45 kg: Initiate rifampin (RIF) 600 mg daily for four months. If less than 45 kg., initiate 10 mg/kg of body weight daily for four months, rounding up to the nearest 150 mg.
- f. For children (less than 12 years of age): Initiate rifampin (RIF) 20 mg/kg of body weight (maximum 600 mg) daily for four months. (For children under 5 years of age contact physician for specific treatment and monitoring orders)
- g. Always calculate mg/kg and then round up to the next available dose.
- h. Review all medications the patient is currently taking with a doctor, pharmacist or a drug, drug interaction product to determine if there are any contraindications to rifampin.
- i. If the patient is on a medication that will interact with rifampin, is allergic or intolerant of rifampin, or is a contact to a rifampin resistant case of tuberculosis, consult physician for treatment orders.
- j. **Hold therapy if signs or symptoms of hepatotoxicity are present (nausea, vomiting, loss of appetite, dark urine, jaundice, malaise, and abdominal discomfort); draw hepatic function panel and consult physician.**
- k. **Hold therapy if there are signs and symptoms of immunologic reactions such as, fever, easy bleeding or bruising, or low hemoglobin (< 13.5 for men, < 12.5 for women, and < 11 for children (less than 12 years)). Draw CBC with platelets and consult physician.**

Nursing Action:

- a. Advise the patient of common adverse reactions to rifampin.
- b. Advise the patient to hold medications and contact the health department if adverse reactions such as, nausea, vomiting, loss of appetite, dark urine, jaundice, malaise, abdominal discomfort, skin rash, fever, easy bleeding or bruising, or low hemoglobin (< 13.5 for men, < 12.5 for women, and < 11 for children (less than 12 years) occur.
- c. Ensure that physician reviews laboratory results and documents this per the agency policy on reviewing laboratory results. (Agency should list the name of this policy here)

Criteria for calling the Physician:

- a. If the patient develops side effects from the medications such as, nausea, vomiting, loss of appetite, dark urine, jaundice, malaise, abdominal discomfort, skin rash, fever, easy bleeding or bruising, or low hemoglobin (< 13.5 for men, < 12.5 for women, and < 11 for children (less than 12 years) occur.
- b. If the patient becomes pregnant.
- c. If the hepatic function or CBC with platelets laboratory results are outside the normal limits.
- d. If there is any question about whether to implement the standing order.

Follow-up Requirements:

- a. Evaluate the patient monthly by completing the Tuberculosis Flow Sheet (DHHS 2810).
- b. Recalculate medication dosage monthly after weighing

Resources: NC TB Control Program Policy Manual 2018 edition.

Legal Authority: Nurse Practice Act, G.S. 90-171.20 (7) (f) & (8) (c)

Date written: _____

Approved by: _____

Date: _____

Approved by: _____

Date: _____

Sample Standing Order: Evaluation and Treatment of Latent Tuberculosis (TB) Infection Using Isoniazid

Assessment: All PHNs employed or contracted by the agency who have completed a TB program orientation will initiate the following standing orders for the evaluation and treatment of latent TB infection using isoniazid (INH) if the patient denies a-j under the subjective findings and a-e under the objective findings and f-i of the objective findings are present.

Subjective findings:

Patient denies the following:

- a. Productive cough, fever, night sweats, weight loss, loss of appetite, shortness of breath, chest pain, and unexplained fatigue;
- b. Completing treatment of latent tuberculosis infection (a minimum of 6 months of isoniazid or 4 months of rifampin or a minimum of 11 doses of isoniazid with rifapentine).
- c. History of hepatitis or liver disease.
- d. History of adverse reaction to isoniazid.
- e. Excess/binge alcohol use (Average alcohol use of \geq three drinks per day or binge drinking (\geq five drinks in one day, sporadically) (one drink is defined as one 12 oz beer, 4 oz of wine or 1 oz of liquor).
- f. Being pregnant or up to 3 months postpartum.
- g. Being exposed to a drug resistant case of TB.
- h. Being on potentially hepatotoxic drugs.
- i. Taking medication that may interact with isoniazid.
- j. Having nausea, vomiting, loss of appetite, dark urine, jaundice, malaise, abdominal discomfort, skin rash, or fever.

Objective findings:

- a. The chest X-ray is not suggestive of previous TB.
- b. The individual is not HIV positive
- c. Is not on hemodialysis.
- d. Is not taking methotrexate.
- e. The baseline or follow-up lab work is not abnormal.
- f. Is $>$ 2 years old but less than 5 years old and a contact to an infectious TB case and treatment needs to be started in the window period between the initial negative TST and the repeat 8 weeks later. **OR**
- g. The TST reaction is \geq 5 mm or has a positive IGRA and meets any of the following criteria:
 - Contact to known or suspected infectious TB disease within the past two years
 - Fibrotic changes on chest radiograph consistent with prior TB disease who have received no or inadequate prior treatment for active TB

- Immunocompromised individuals, e.g., receiving ≥ 15 mg per day of Prednisone for 1 mo., other immunosuppressive drugs, organ transplant, or people taking or considering taking tumor necrosis factor (TNF) inhibitors like etanercept (Embrel®), infliximab (Remicade®) or anakinra (Kineret™) or adalimumab (Humira®) **OR**

The TST reaction is ≥ 10 mm or has a positive IGRA and meets any of the following criteria:

- Foreign-born individuals from Asia, Africa, Caribbean, Latin America, Mexico, South America, Pacific Islands or Eastern Europe
Low prevalence countries are USA, Canada, Japan, Australia, Western Europe, and New Zealand
 - Those who have converted their TST within two years
 - Those with medical conditions which place them at high risk for TB disease
 - Diabetes mellitus
 - Chronic renal failure
 - Chronic malabsorption syndrome
 - Leukemia, lymphomas, Hodgkin's disease
 - Cancer of the head or neck
 - Silicosis
 - Weight loss of $\geq 10\%$ ideal body weight
 - Gastrectomy or intestinal bypass
 - Injection drug or crack cocaine user
 - Children < 4 years of age
 - Children and adolescents exposed to high risk adults
 - People residing for > 1 month in a high incidence area
 - Mycobacteriology lab personnel
 - Residents of homeless shelters
 - Prison inmates and personnel
 - Jail personnel
 - Healthcare personnel
- h. No mycobacterial (AFB) cultures pending or all AFB culture are reported as negative for *Mycobacterium tuberculosis (M. tuberculosis)*.
- i. Chest X-ray interpretation does not indicate evidence of active TB disease.

Plan of Care:

1. Implementation:

- If the patient has anything listed under subjective a-j or objective a-e or has a positive TST or IGRA but has no risk factors for progression to TB do not engage the standing order and consult with the physician for specific orders.
- Obtain posterior-anterior (PA) view chest X-ray, additionally:
 - Use appropriate shielding for pregnant women,
 - If a patient had a previously documented positive TST/IGRA and a negative PA chest X-ray within the last two years, the chest X-ray does not need to be repeated if the patient reports no symptoms of active TB.

- c. A chest X-ray taken within the past three months is required for asymptomatic new converters, HIV positive individuals, and those who are taking medication that cause immunosuppression.
- d. Children under age five should also have a lateral view chest X-ray.
- c. Complete Tuberculosis Epidemiological Record (DHHS 1030).
- d. Obtain HIV test unless the patient specifically refuses or has documentation of testing with the past 6 months.
- e. For adults (greater than 12 years of age): Initiate Isoniazid (INH) 5 mg/kg (maximum 300 mg) daily for six months.
- f. For children (less than 12 years of age): Initiate Isoniazid (INH) 10 mg/kg (maximum 300 mg) daily for six months.
- g. Always calculate mg/kg and then round up to then next available dose.
- h. Initiate Pyridoxine (B6) 25 mg per day along with INH if the patient is an adult and has any of the following conditions:
 - a. Diabetes
 - b. Alcohol use of > 3 drinks per day
 - c. Malnutrition
 - d. Seizure disorder
- i. Review all medications the patient is currently taking with a doctor, pharmacist or a drug, -drug interaction product to determine if there are any contraindications to co-administration of isoniazid with the patient's current medications.
- j. If the patient is on a medication that will interact with isoniazid, is allergic or intolerant of isoniazid, or is a contact to an isoniazid resistant case of tuberculosis contact the physician for an alternate treatment.
- k. **Hold therapy if signs or symptoms of hepatotoxicity are present (nausea, vomiting, loss of appetite, dark urine, jaundice, malaise, and abdominal discomfort); draw hepatic function panel and consult physician.**

Nursing Action:

- a. Advise the patient of common adverse reactions to isoniazid.
- b. Advise the patient to hold medications and contact the health department if adverse reactions such as, nausea, vomiting, loss of appetite, dark urine, jaundice, malaise, abdominal discomfort, skin rash, or fever occurs.
- c. Ensure that physician reviews laboratory results and documents this per the agency policy on reviewing laboratory results. (Agency should list the name of this policy here)

Criteria for calling the Physician:

- a. If the patient develops side effects from the medications such as, nausea, vomiting, loss of appetite, dark urine, jaundice, malaise, abdominal discomfort, skin rash, fever, or if numbness or tingling of the hands or feet occur.
- b. If the patient becomes pregnant.
- c. If the hepatic function laboratory results are outside the normal limits.
- d. If there is any question about whether to implement the standing order.

Follow-up Requirements:

- a. Evaluate the patient monthly by completing the Tuberculosis Flow Sheet (DHHS 2810).
- b. Recalculate medication dosage monthly after weighing

Resources: NC TB Control Program Policy Manual 2018 edition.

Legal Authority: Nurse Practice Act, G.S. 90-171.20 (7) (f) & (8) (c)

Date written: _____

Approved by: _____

Date: _____

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Date: _____