## III. Targeted Testing and Treatment of Latent Tuberculosis Infection (LTBI)

A. The following individuals have a relatively high risk for progressing to TB disease and therefore should be given high priority for treatment for LTBI **regardless of age:**

| TST≥ 0mm | TST≥ 5mm | TST≥ 10mm | TST≥ 15mm | Positive IGRA |
|---|---|---|---|---|
| HIV-positive or other severely immuno-compromised individuals (e.g. solid organ or bone marrow transplant) who are recent contacts to known or suspected infectious TB disease, regardless of previous treatment of LTBI<br><br>HIV-positive with fibrotic changes on CXR consistent with prior TB who have received inadequate or no treatment for TB disease<br><br>Children < 5 years of age identified as a recent contact to known or suspected infectious TB disease | HIV-positive<br><br>Contacts to known or suspected infectious TB disease identified within the past two years<br><br>Those with fibrotic changes on CXR consistent with prior TB and have received inadequate or no treatment for TB disease<br><br>Immunocompromised individuals, e.g., receiving ≥ 15 mg per day of Prednisone for 1 mo., other immunosuppressive drugs, organ transplant, or persons taking or considering taking tumor necrosis factor (TNF) inhibitors like etanercept (Embrel ®), infliximab (Remicade ®) or anakinra (Kineret™) or adalimumab (Humira ®) | Foreign-born individuals from Asia, Africa, Caribbean, Latin America, Mexico, South America, Pacific Islands or Eastern Europe<br>*Low prevalence countries are USA, Canada, Japan, Australia, Western Europe, and New Zealand*<br><br>Those who have converted their TST within two years<br><br>Those with medical conditions which place them at high risk for TB disease<br>• diabetes mellitus<br>• chronic renal failure<br>• chronic malabsorption syndrome<br>• leukemia, lymphomas, Hodgkin's disease<br>• cancer of the head or neck<br>• silicosis<br>• weight loss of ≥ 10% ideal body weight<br>• gastrectomy or intestinal bypass<br><br>Injection drug or crack cocaine user<br><br>Children < 4 years of age<br><br>Children and adolescents exposed to high risk adults<br><br>Persons staying for > 1 month with someone in a high incidence area<br><br>Mycobacteriology lab personnel<br><br>**The following individuals are at a lower risk for developing TB disease and are candidates for TLTBI if local resources are sufficient and the benefits outweigh the risk:**<br><br>○ Residents of long-term care facilities, and homeless shelters<br>○ Inmates in the DOC<br>○ Personnel in the following settings:<br>• Prisons<br>• Jails<br>• Long-term care facilities<br>• Hospitals and other health care facilities<br>• Adult day care centers for HIV positive/AIDS<br>• Homeless shelters | Persons with no risk factors for TB | Persons with a positive interferon gamma release assay (IGRA) regardless of risk factors/exposures should also be considered at risk to develop active TB disease, and should be offered LTBI treatment. |

TST=tuberculin skin test; IGRA=interferon gamma release assay

B. Targeted testing identifies individuals at high-risk for developing TB who would benefit from treatment of LTBI. 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. Treatment of LTBI presumably acts by diminishing the bacterial population in healed or radiographically invisible lesions.

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. All persons with LTBI should be offered HIV testing, regardless of perceived risk for HIV infection.

3. A review for symptoms of disease and a chest x-ray to exclude active tuberculosis disease are required before starting any treatment for latent infection:
   - A chest x-ray taken within the past two years is acceptable for asymptomatic HIV negative individuals with a remote positive TST; and
   - A chest x-ray taken within the past three months is required for asymptomatic new converters, HIV+ individuals, and those who are severely immunocompromised.
   - PA and Lateral views should be obtained on children less than 5.

4. If the patient reports a cough and sputum results are pending, wait until sputum culture results are reported as negative before starting medications.

5. Obtain a medical history including 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 INH or RIF.

7. Directly Observed Preventive Therapy (DOPT) should generally be used with all regimens administered once or twice weekly, although in selected cases (e.g. INH and rifapentine in patients with expected good adherence), self-administration is acceptable. DOPT is strongly recommended for:
   - Those with HIV infection;
   - Children < 5 years of age; and
   - Infected close contacts to isoniazid (INH) or rifampin (RIF) resistant TB.

8. Certain TB drugs should be calculated according to mg/kg body weight. Calculate on the lower figure in the range and round up to the next available dose supplied by the manufacturer **(see Chapter VI for dosage table).**

9. The health care provider or an interpreter should be conversant in the patient's own language to ensure good communication.

10. All patients should be instructed to stop their medication and seek immediate medical consultation if they experience loss of appetite, abdominal pain, nausea, vomiting, jaundice or other symptoms of hepatitis.

11. All patients must be clinically assessed at least monthly for adverse reactions and the findings documented **(see TB Flow Sheet – DHHS 2810).**

12 The appropriate drug information fact sheet(s) should be reviewed with the patient.

13 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 in this chapter; section K. Your TB Medical Director 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

D. Standard Regimens for HIV Negative Adults ≥ 15 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 at a dose of 15 mg/kg (maximum 900 mg), plus 15 mg/kg of rifapentine (maximum 900 mg), given together once weekly for 12 weeks, taken within a 16 week period of time. Missed doses can still be administered up to 72 hours before the next dose.
- Regimen is contraindicated for pregnant and breastfeeding women.
- Rifapentine interacts with many other drugs. Please see Chapter VI of the NC TB Control Manual for a *partial* list of drugs that interact with rifapentine.
- With approval of the local TB clinician, self-administered isoniazid and rifapentine is acceptable. Directly observed preventive therapy should be reserved for persons 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 INH;
     - Individual is a close contact to INH-resistant, RIF-susceptible TB;
   - RIF 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**.
   - Dosage for RIF is calculated according to body weight and rounded up to the next available dose. 10 mg/kg per day with a daily maximum of 600 mg.
   - Daily RIF (120 doses) should be given for a total of four months within a six-month period of time
   - **RIF by itself may not be given on a twice-weekly schedule**.

3. Isoniazid for nine months
   - Nine months of INH should be offered to patients with intolerance to rifampin/rifapentine or unacceptable drug interactions with rifampin/rifapentine
   - Dosage for INH is 5 mg/kg (maximum 300mg) daily (270doses) or 15mg/kg (maximum 900mg) twice-weekly DOPT (78 doses) for a total of nine months to be taken within a 12-month period of time.

- INH 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.

4. Isoniazid for six months:
    - Six months of INH offers an acceptable degree of protection against the progression of TB infection to TB disease (approximately 70 percent in individuals who complete a full course of therapy)
    - Dosage for INH is 300 mg daily (180 doses) or 900 mg twice-weekly DOPT (52 doses) for a total of 6 months to be taken within a nine-month period of time.
    - Six months of INH will be considered an adequate course of treatment for LTBI when nine months cannot be completed.
    - INH 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.

E. Standard Adult Regimens for Inadequately or Untreated Previous TB

1. Individuals with a chest x-ray suggestive of fibrotic lesions thought to represent previous TB and positive Interferon Gamma Release Assay (IGRA) or TST (≥ 5mm) should be treated for LTBI after active TB disease has been ruled out. Treatment options are:
    - INH plus rifapentine once-weekly for 12 weeks (directly observed or self-administered)
    - RIF (with or without INH) for four months. **RIF by itself must be taken daily**
    - INH for nine months

2. Individuals with chest x-rays suggestive of healed primary TB disease (i.e. calcified solitary pulmonary nodules, calcified hilar lymph nodes, and apical pleural scarring) and positive IGRA or TST (≥ 5mm) are not at increased risk for TB disease. The need for treating LTBI in healed primary TB disease should be determined by:
    - Size of the TST; and
    - Risk factors for progression to disease.

F. Standard Regimens for HIV-Negative Infants and Children (< 15 Years)

1. Three months of once-weekly isoniazid-rifapentine (12 doses)
    - 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
    - Isoniazid is administered at a dose of 20 mg/kg (maximum 900 mg), plus 20 mg/kg of rifapentine (maximum 900 mg), both rounding up to the next available dose, given together once weekly for 12 weeks, taken within a 16 week period of time.
    - Children weighing more than 40 kg should be dosed as an adult.
    - Missed doses can still be administered up to 72 hours before the next dose.

- Rifapentine interacts with many other drugs. Please see Chapter VI of the NC TB Control Manual for a *partial* list of drugs that interact with rifapentine.
- Note that 11 doses taken within 16 weeks is adequate for completion of INH/Rifapentine treatment.

2. Four months of rifampin (120 doses).
   - This regimen is a preferred option for latent TB treatment in children, especially in the following circumstances
     - Intolerance to INH;
     - Individual is a close contact to INH-resistant, RIF-susceptible TB
     - Children under 2 years of age
   - Dosage for RIF is 15-20 mg/kg, rounding up to the next available dose, daily (120 doses) for a total of 4 months taken within a six-month period of time
   - **RIF by itself may not be given on a twice-weekly schedule.**
   - RIF 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. Nine months of isoniazid
   - Nine months of INH should be offered to patients with intolerance to rifampin/rifapentine or unacceptable drug interactions with rifampin/rifapentine
   - Dosage for INH is calculated according to body weight and rounded up to the next available dose. Dosage is 10 mg/kg for daily dose (maximum 300 mg) and 20 mg/kg (maximum 900 mg) for twice weekly dose.
   - Daily INH (270 doses) or twice-weekly DOPT (78 doses) should be given for a total of nine months within a 12-month period of time.

**Weigh child at least monthly and adjust dosage as weight changes**

G. Standard Regimens for HIV-Negative 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 INH or RIF during pregnancy with appropriate monitoring.

4. Treatment Regimens

a. 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 INH-resistant, RIF-susceptible TB;
   - Individual is high-risk for progression to active TB but is unlikely to adhere to a full nine-month course of INH; and
   - Individual is at relatively high risk for hepatotoxicity from INH (e.g. excess alcohol use, concurrent hepatotoxic medication).
   - RIF 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.
   - Dosage for RIF is calculated according to body weight and rounded up to the next available dose. 10 mg/kg per day with a daily maximum of 600 mg.
   - Daily RIF (120 doses) should be given for a total of four months within a six-month period of time.
   - **<u>RIF by itself may not be given on a twice-weekly schedule.</u>**

b. Isoniazid for nine months:
   - INH is an acceptable regimen for pregnant women who cannot take rifampin due to intolerance or drug interactions
   - Dosage for INH is 300mg daily (270 doses) or 900mg twice-weekly DOPT (78 doses) for a total of nine months to be taken within a 12 month period of time;
   - Six months of INH given within a 9 month period of time will be considered an adequate course of treatment for LTBI when nine months cannot be completed; and
   - INH 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.

H. <u>Pyridoxine</u>

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

2. Pyridoxine ($B_6$) 25 mg. daily or 50 mg. twice weekly (once weekly with INH/rifapentine) should be given on the same schedule with INH if 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 $B_6$; and
   f. Seizure disorder.

3. Individuals who develop peripheral neuropathy while taking daily $B_6$ should have their $B_6$ dose doubled. If neuropathy is not resolved in two weeks, consult physician.

4. Individuals on dialysis should be given $B_6$ 50mg on the same schedule with INH.

5. Pyridoxine ($B_6$) 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 (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. Frequency:
      - Daily.

   c. 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.

   d. 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.

I. <u>Monitoring of LTBI</u>

1. INH monitoring

   a. Prior to initiating INH, obtain a baseline hepatic function panel[1] (includes: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and total bilirubin) on the following individuals:
      - Average alcohol use of ≥three drinks per day or binge drinking (≥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)
    - cerivastatin (Baycol)
    - 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. Obtain hepatic function panel[2] monthly on the following individuals who are taking INH:
- 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);

1. 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. RIF monitoring

a. Prior to initiating RIF, obtain a baseline CBC with platelets, and hepatic function panel[1] on the following individuals:

[1] Note that this is an incomplete list of drugs with potential for hepatotoxicity
[2] Hepatic Function Panel includes: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and total bilirubin.

- average alcohol use of ≥ three drinks per day or binge drinking (≥ 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:[1]
  - ♦ "statin" drugs;
    - atorvastatin (Lipitor)
    - cerivastatin (Baycol)
    - 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 panel[2] monthly on the following individuals who are taking RIF only:
- 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);

2. Those with symptoms of adverse reactions;

- Persons taking potentially hepatotoxic drugs (above list);
- Persons with chronic active hepatitis B or those with hepatitis C;
- Chronic or binge use of alcohol; and
- Those with HIV infection.

**Hold therapy if <u>signs or symptoms</u> 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

a. Prior to initiating INH/rifapentine, obtain a baseline hepatic function panel[1] (includes: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and total bilirubin) and complete blood count (CBC) with platelets on the following individuals:

[1] Note that this is an incomplete list of medications with potential for hepatotoxicity

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

- Average alcohol use of ≥ three drinks per day or binge drinking (≥ 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.
- Those currently taking other potentially hepatotoxic drugs such as:[1]
  - ♦ "statin" drugs;
    - atorvastatin (Lipitor)
    - cerivastatin (Baycol)
    - 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 INH/RPT 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).

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

c. Obtain hepatic function panel[2] monthly on the following individuals who are taking INH/RPT:
- 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);

3. Those with symptoms of adverse reactions;

- Persons taking potentially hepatotoxic drugs (above list);
- Persons with chronic active hepatitis B or those with hepatitis C;
- Chronic or binge use of alcohol; and
- Those with HIV infection.

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

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

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 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.

J. Closure of Patient Record for Non-Adherence

a. Contact patient by telephone within 14 days of failure to pick up medication.
b. If unable to reach by phone or no response to call, send a letter identifying the benefits of TLTBI and symptoms of tuberculosis disease; advise patient to contact you within two weeks (give date) or record will be closed.
c. If no response to letter or patient refuses treatment, close patient's record to follow-up.

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-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 rifampin, rifapentine or isoniazid.
e. Excess/binge alcohol use (Average alcohol use of ≥three drinks per day or binge drinking (≥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, 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. The tuberculin skin test is interpreted as positive (based on guidance from page 1 of chapter 3 of the NC TB Control Manual 2012 edition), or an interferon gamma release assay (IGRA) for TB is reported as positive.
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 patent has anything listed under subjective a-j or objective a-f 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 15 years of age) initiate Isoniazid 15 mg/kg (maximum 900 mg), plus 15 mg/kg of rifapentine (maximum 900 mg), given together once weekly for 12 weeks, taken within a 16 week period of time.
f. For HIV negative children (ages 2-14, inclusive): initiate isoniazid 20 mg/kg (maximum 900 mg), plus 20 mg/kg of rifapentine (maximum 900 mg), given together once weekly for 12 weeks, taken within a 16 week period of time.
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 <u>signs or symptoms</u> 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 15 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 15 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 15 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-f under the objective findings and g-I of the objective findings are present.

**Subjective findings:**
Patient denies the following:

k. Productive cough, fever, night sweats, weight loss, loss of appetite, shortness of breath, chest pain, and unexplained fatigue;
l. 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).
m. History of hepatitis or liver disease.
n. History of adverse reaction to rifampin.
o. Excess/binge alcohol use (Average alcohol use of ≥three drinks per day or binge drinking (≥five drinks in one day, sporadically) (one drink is defined as one 12 oz beer, 4 oz of wine or 1 oz of liquor).
p. Being pregnant or up to 3 months postpartum.
q. Being exposed to a drug resistant case of TB.
r. Being on potentially hepatotoxic drugs.
s. Taking medication that may interact with rifampin.
t. Having nausea, vomiting, loss of appetite, dark urine, jaundice, malaise, abdominal discomfort, skin rash, fever, or unexplained bruising/bleeding.

**Objective findings:**

j. The chest x-ray is not suggestive of previous TB.
k. The individual is not HIV positive
l. Is not on hemodialysis.
m. Is not taking methotrexate.
n. Is not a child less than 5 years old.
o. The baseline or follow-up lab work is not abnormal.
p. The tuberculin skin test is interpreted as positive (based on guidance from page 1 of chapter 3 of the NC TB Control Manual 2012 edition), or an interferon gamma release assay (IGRA) for TB is reported as positive.
q. No acid fast bacterium (AFB) culture pending or all AFB cultures are reported as negative for Mycobacterium tuberculosis (M.tb).
r. Chest x-ray interpretation does not indicate evidence of active TB disease.

**Plan of Care:**

2. **Implementation:**
   a. If the patent has anything listed under the subjective a-j or the objective findings a-f 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 15 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 15 years of age): Initiate rifampin (RIF) 15 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 does.
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 <u>signs or symptoms</u> 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 15 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 15 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 15 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-f under the objective findings and g-I of the objective findings are present.

**Subjective findings:**
Patient denies the following:

u. Productive cough, fever, night sweats, weight loss, loss of appetite, shortness of breath, chest pain, and unexplained fatigue;
v. 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).
w. History of hepatitis or liver disease.
x. History of adverse reaction to isoniazid.
y. Excess/binge alcohol use (Average alcohol use of ≥three drinks per day or binge drinking (≥five drinks in one day, sporadically) (one drink is defined as one 12 oz beer, 4 oz of wine or 1 oz of liquor).
z. Being pregnant or up to 3 months postpartum.
aa. Being exposed to a drug resistant case of TB.
bb. Being on potentially hepatotoxic drugs.
cc. Taking medication that may interact with isoniazid.
dd. Having nausea, vomiting, loss of appetite, dark urine, jaundice, malaise, abdominal discomfort, skin rash, or fever.

**Objective findings:**

s. The chest x-ray is not suggestive of previous TB.
t. The individual is not HIV positive
u. Is not on hemodialysis.
v. Is not taking methotrexate.
w. The baseline or follow-up lab work is not abnormal.
x. The tuberculin skin test is interpreted as positive (based on guidance from page 1 of chapter 3 of the NC TB Control Manual 2018 edition), or an interferon gamma release assay for TB is reported as positive.
y. No acid fast bacterium (AFB) culture pending or all AFB culture are reported as negative for Mycobacterium tuberculosis (M.tb).
z. Chest x-ray interpretation does not indicate evidence of active TB disease.

**Plan of Care:**

3. **Implementation:**
   b. If the patent has anything listed under subjective a-j or objective a-f do not engage the standing order and consult with the physician for specific orders.
   c. 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 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.

d. Complete Tuberculosis Epidemiological Record (DHHS 1030).
e. Obtain HIV test unless the patient specifically refuses or has documentation of testing with the past 6 months.
f. For adults (greater than 15 years of age): Initiate Isoniazid (INH) 5 mg/kg (maximum 300 mg) daily for nine months.
g. For children (less than 15 years of age): Initiate Isoniazid (INH) 10 mg/kg (maximum 300 mg) daily for nine months.
h. Always calculate mg/kg and then round up to then next available dose.
i. Initiate Pyridoxine (B6) 25 mg per day along with INH if the patient is an adult and has any of the following conditions:
    - Diabetes
    - Alcohol use of > 3 drinks per day
    - Malnutrition
    - Seizure disorder
j. 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.
k. If the patient is on a medication that will interact with is 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.
l. **Hold therapy if <u>signs or symptoms</u> 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.

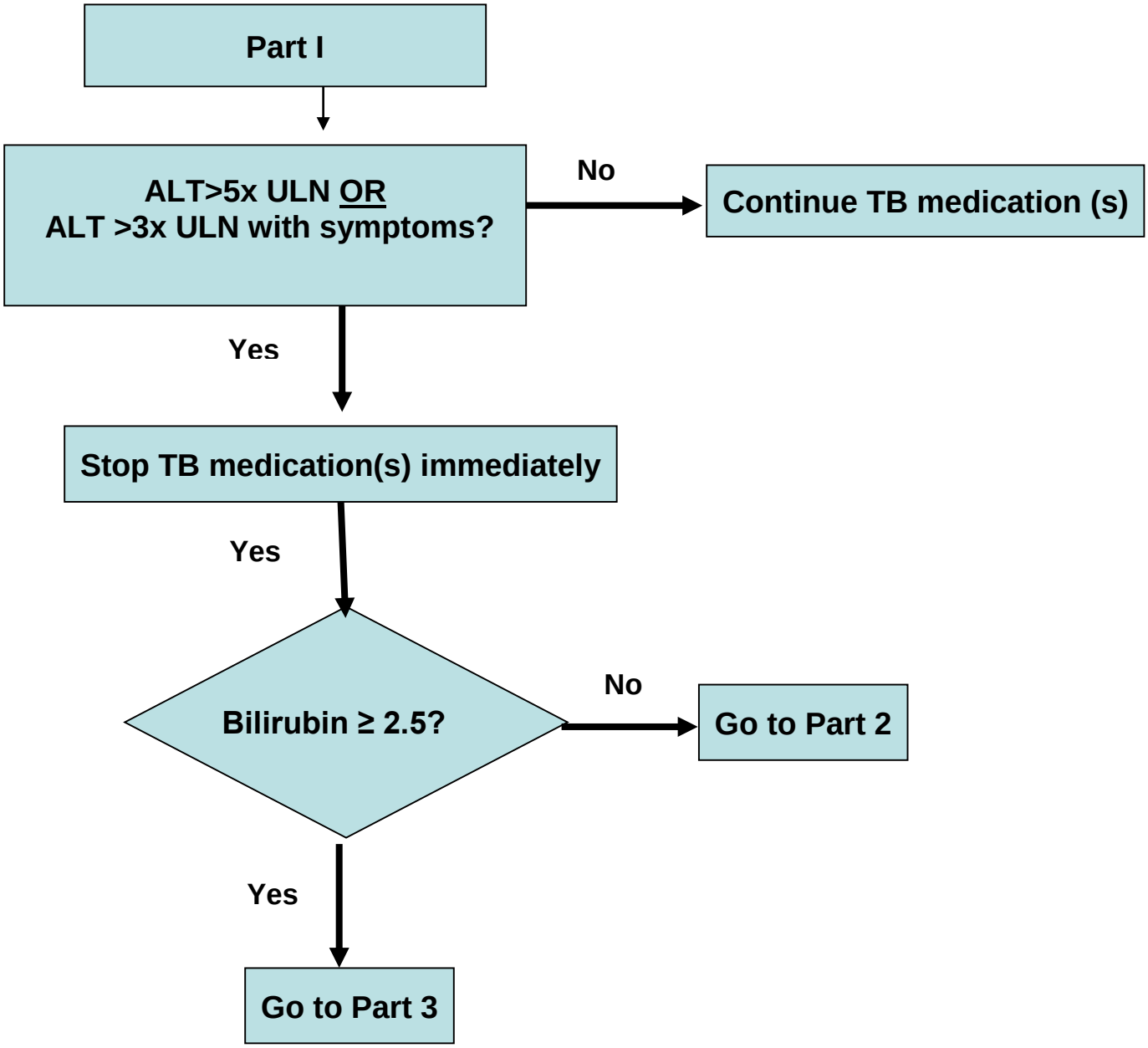
**Legal Authority:** Nurse Practice Act, G.S. 90-171.20 (7) (f) & (8) (c)

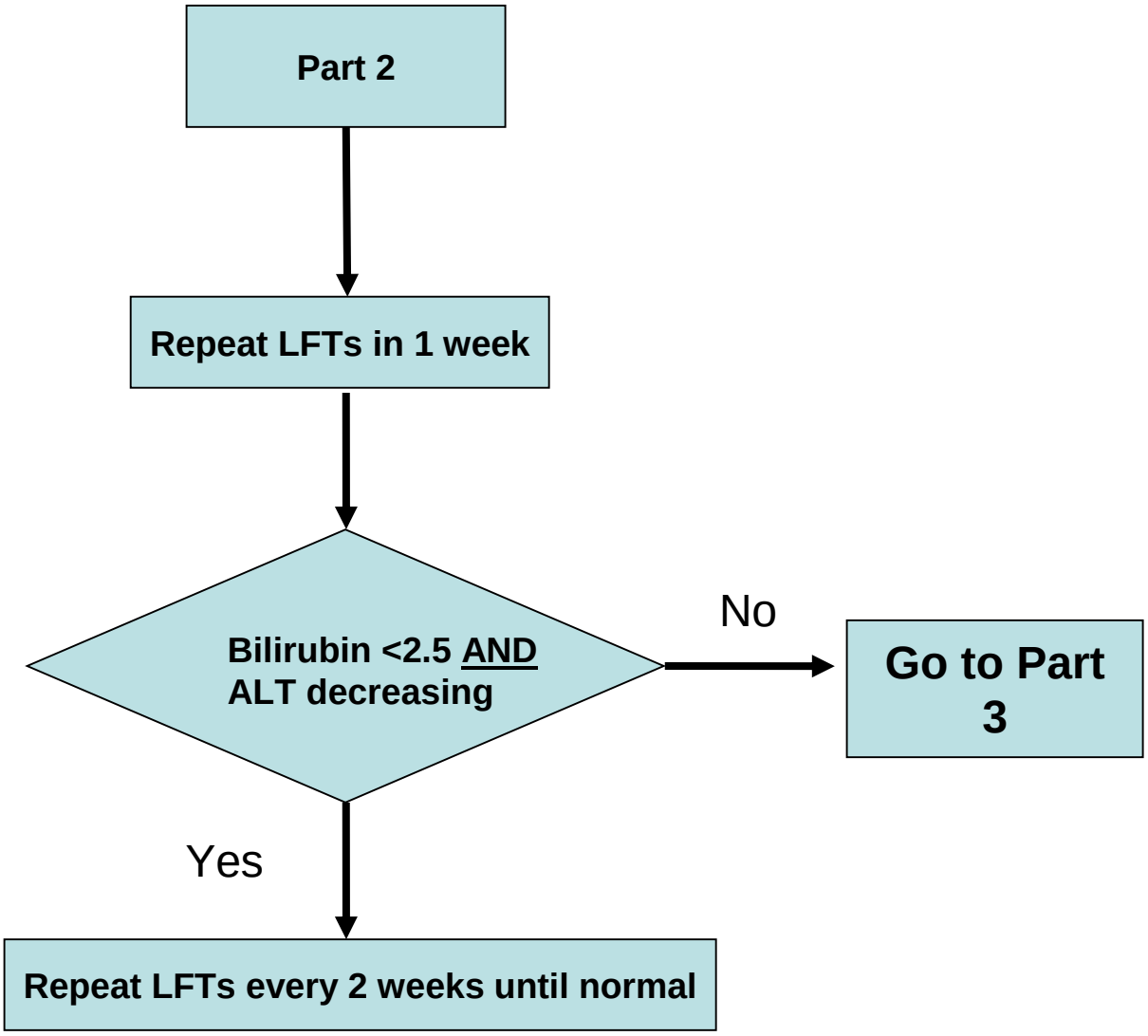
Date written:_____

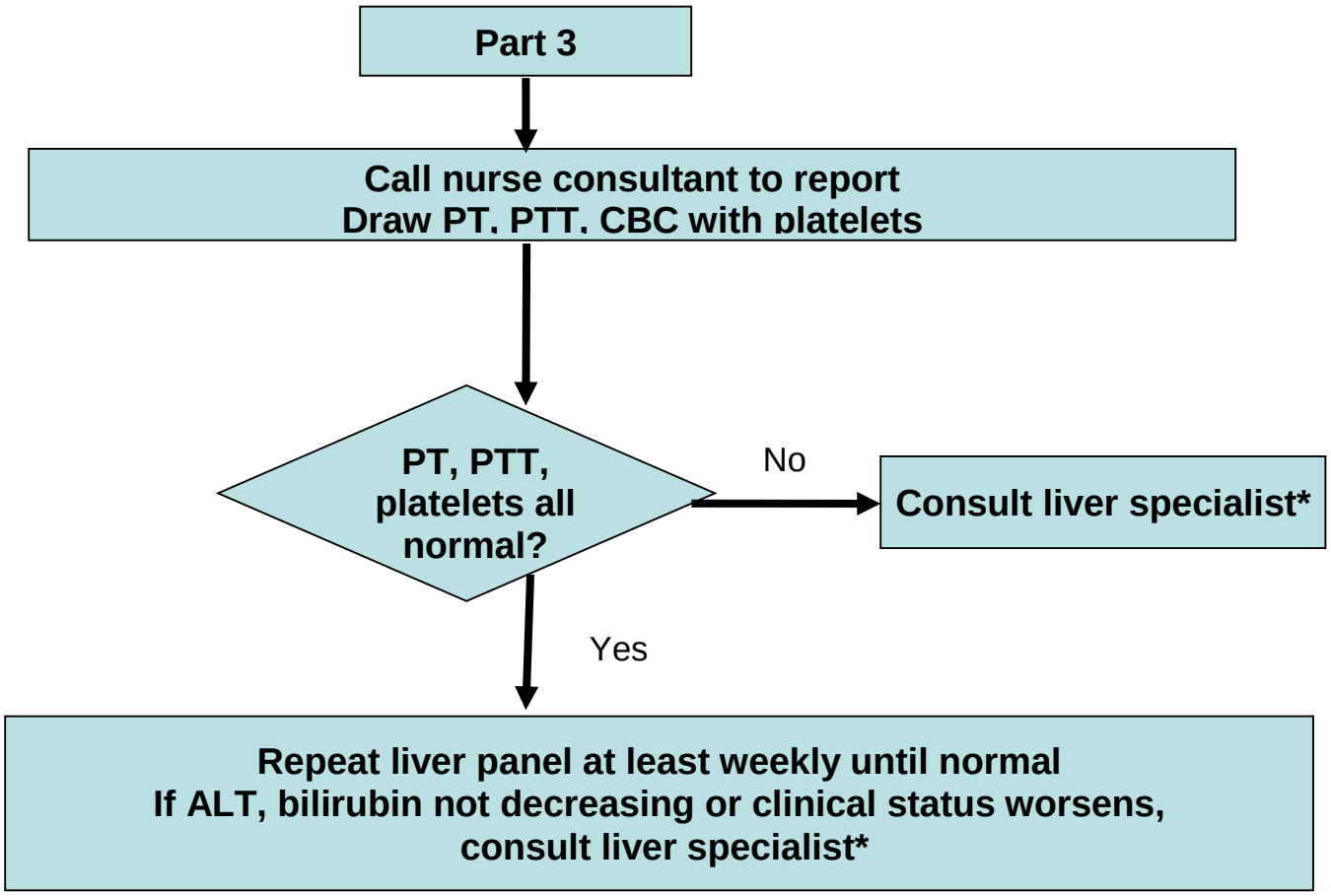
Approved by: _____ Date:_____

Approved by: _____ Date:_____

L. Hepatotoxicity Flowchart




Part 2
Repeat LFTs in 1 week
Bilirubin <2.5 AND
ALT decreasing
No
Go to Part 3
Yes
Repeat LFTs every 2 weeks until normal




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