

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:**

≥ 0mm	≥ 5mm	≥ 10mm	≥ 15mm
<p>HIV-positive or other immunocompromised individuals who are recent contacts to known or suspected infectious TB disease, regardless of previous treatment of LTBI</p> <p>HIV-positive with fibrotic changes on CXR consistent with prior TB who have received inadequate or no treatment for TB disease</p> <p>Children < 5 year of age identified as a recent contact to known or suspected infectious TB disease</p>	<p>HIV-positive</p> <p>Contacts to known or suspected infectious TB disease identified within the past 2 years</p> <p>Those with fibrotic changes on CXR consistent with prior TB and have received inadequate or no treatment for TB disease</p> <p>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®)</p>	<p>Foreign-born individuals from Asia, Africa, Caribbean, Latin America, Mexico, South America, Pacific Islands or Eastern Europe <i>Low prevalence countries are USA, Canada, Japan, Australia, Western Europe, and New Zealand</i></p> <p>Those who have converted their TST within 2 years</p> <p>Those with medical conditions which place them at high-risk for TB disease</p> <ul style="list-style-type: none"> • diabetes mellitus • chronic renal failure • chronic malabsorption syndrome • leukemia, lymphomas, Hodgkin's disease • cancer of the head or neck • silicosis • weight loss of ≥ 10% ideal body weight • gastrectomy or intestinal bypass <p>Injection drug or crack cocaine user</p> <p>Children < 4 year of age</p> <p>Children and adolescents exposed to high risk adults</p> <p>Persons staying for > 1 month with someone in a high incidence area</p> <p>Mycobacteriology lab personnel</p> <p>The following individuals are at a lower risk for developing TB disease and are candidates for TLTI if local resources are sufficient and the benefits outweigh the risk:</p> <ul style="list-style-type: none"> ○ Residents of long-term care facilities, and homeless shelters ○ Inmates in the DOC ○ Employees in the following settings: <ul style="list-style-type: none"> • Prisons • Jails • Long-term care facilities • Hospitals and other health care facilities • Adult day care centers for HIV positive/AIDS • Homeless shelters 	<p>Persons with no risk factors for TB</p>

- 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. 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 2 years is acceptable for asymptomatic HIV negative individuals with a remote positive PPD
 - a chest x-ray taken within the past 3 months is required for new converters, HIV+ individuals, and those who are severely immunocompromised
 3. 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**)
 4. TB medications in institutional/congregate settings should be administered daily by direct observation
 5. For self administration, never give more than a 30 day supply of INH or RIF
 6. Directly Observed Preventive Therapy (DOPT) must be used with all regimens administered twice weekly. DOPT is strongly recommended for:
 - those with HIV infection
 - children < 15 years of age
 - infected close contacts to isoniazid (INH) or rifampin (RIF) resistant TB
 7. 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 IV for dosage table**)
 8. The health care provider or an interpreter should be conversant in the patient's own language to ensure good communication
 9. *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.*
 10. All patients must be clinically assessed at least monthly for adverse reactions and the findings documented (**see TB Flow Sheet – DHHS 2810**)
 11. The TB Epidemiological Record (**DHHS 1030**) should be signed by the patient for verification of understanding

12. Health department TB nurses may manage latent TB infection under standing orders signed by a physician or contract TB clinician. (see Chapter III, page 8 for an example of standing orders)

D. Standard Regimens for HIV Negative Adults ≥ 15 Years

1. INH for 9 months is the preferred regimen
 - 9 months of INH offers the highest degree of protection against the progression of TB infection to TB disease (approximately 90% in individuals who complete a full course of therapy)
 - 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 9 months to be taken within a 12-month period of time
 - INH for LTBI is contraindicated for individuals with active hepatitis or end-stage liver disease
2. INH for 6 months
 - 6-month regimen of INH offers an acceptable degree of protection against the progression of TB infection to TB disease (approximately 70% 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 9-month period of time
 - 6 months of INH will be considered an adequate course of treatment for LTBI when 9 months cannot be completed
 - INH for LTBI is contraindicated for individuals with active hepatitis or end-stage liver disease
3. 4 months of RIF should be offered only if intolerance to INH develops or the individual is a close contact to INH resistant-RIF susceptible case of TB
 - dosage for RIF is calculated according to body weight and rounded up to the next available dose
 - daily RIF (120 doses) should be given for a total of 4 months within a 6-month period of time (the 4-month regimen is only for those ≥ 15 years of age)
 - RIF by itself may not be given on a twice-weekly schedule
4. RIF-PZA
 - RIF-PZA for treatment of latent TB infection is no longer recommended for routine use due to the unacceptable incidence of severe hepatitis resulting in hospitalization, liver transplantation and sometimes death. Only when a strict clinical protocol is being followed under the direction of a physician and has been approved by the NC TB Control Program Medical Director should this regimen be undertaken.
 - **RIF and PZA remain essential elements in the standard regimen for treating active TB disease.**

E. Standard 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 TST (≥ 5mm) should be treated for LTBI after active TB disease has been ruled out. Treatment options are:
 - INH for 9 months, or
 - RIF (with or without INH) for 4 months (RIF by itself must be taken daily)

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 TST (≥ 5 mm) 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. 9 months of INH is the only recommended regimen for treating LTBI in infants and children
 - a. 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 and 20 mg/kg for twice weekly dose.
 - b. Daily INH (270 doses) or twice-weekly DOPT (78 doses) should be given for a total of 9 months within a 12-month period of time
2. 6 months of RIF (180 doses) can be offered only if intolerance to INH develops or the individual is a close contact to an INH resistant-RIF susceptible case of TB
3. RIF by itself may not be given on a twice-weekly schedule
4. Children weighing more than 40 kg should be dosed as an adult

Weigh child at least monthly and adjust dosage as weight changes

G. Standard Regimen 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
2. Asymptomatic TST positive pregnant women with a negative chest x-ray should start INH preventive therapy as soon as possible if they have one of the following factors:
 - HIV infection
 - close contact to infectious TB disease
 - TST conversion
 - high-risk medical condition
3. Asymptomatic TST positive pregnant women with a negative chest x-ray and no risk factors may elect to delay preventive therapy until after delivery
4. Treatment Regimens
 - a. INH for 9 months is the preferred regimen for treating LTBI during pregnancy

- dosage for INH is 300mg daily (270 doses) or 900mg twice-weekly DOPT (78 doses) for a total of 9 months to be taken within a 12 month period of time
 - 6 months of INH will be considered an adequate course of treatment for LTBI when 9 months cannot be completed
 - INH for LTBI is contraindicated for individuals with active hepatitis or end-stage liver disease
- b. RIF is an acceptable alternative for pregnant women intolerant to INH or a contact to INH resistant case of TB; (**RIF by itself must be given on a daily schedule**)
 - c. PZA is contraindicated because its effect on the fetus is unknown
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. Pyridoxine

1. Peripheral neuropathy is associated with the use of INH but is uncommon at doses of 5 mg/kg of body weight
2. Pyridoxine (B₆) 25 mg. daily or 50 mg. twice weekly 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 >3 drinks per day
 - c. malnutrition
 - d. HIV infection
 - e. pregnancy, if prenatal vitamin does not contain at least 25 mg of B₆
 - 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 2 weeks, consult physician.
4. Individuals on dialysis should be given B₆ 50mg on the same schedule with INH
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. Additionally, exclusively breastfed infants whose mothers are taking INH should be offered B₆ as a supplement. Mothers declining B₆ for their infants should not have INH treatment for LTBI withheld.
 - 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.

I. Monitoring of LTBI

1. INH monitoring

- a. Prior to initiating INH, obtain a baseline hepatic function panel on the following individuals:
 - average alcohol use of >3 drinks per day (1 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 3 months postpartum
 - those currently taking other potentially hepatotoxic drugs such as:
 - ◆ "statin" drugs
 - atorvastatin (Lipitor)
 - cerivastatin (Baycol)
 - lovastatin (Mevacor)
 - pravastatin (Pravachol)
 - rosuvastatin (Crestor)
 - simvastatin (Zocor)
 - ◆ anticonvulsant drugs
 - carbamazepine (Tegretol)
 - phenytoin (Dilantin)
 - valproic acid (Depakote)
 - ◆ methotrexate
 - ◆ 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 monthly on the following individuals who are taking INH:
 - 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

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

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

- see page 9 of this chapter for a flowchart on how to address hepatotoxicity in patients taking TB medications
- complete CDC National Surveillance for Severe Adverse Event data collection form (chapter IX, pages 67-71) if the patient has hepatotoxicity severe enough to require hospitalization or death and send to regional nurse consultant

2. RIF monitoring

- Prior to initiating RIF, obtain a baseline CBC with platelets, and hepatic function panel on the following individuals:
 - average alcohol use of >3 drinks per day
 - HIV positive
 - underlying liver disease
 - pregnant women
- If baseline CBC with platelets and liver function panel are outside normal limits, consult physician before initiating treatment for LTBI
- Obtain hepatic function panel monthly on the following individuals who are taking RIF only:
 - baseline results are abnormal
 - those with symptoms of adverse reactions

Hold therapy if signs and symptoms of hepatotoxicity are present; draw hepatic function panel and consult physician.

J. Closure of Patient Record for Non-Adherence

- Contact patient by telephone within 14 days of failure to pick up medication
- If unable to reach by phone or no response to call, send a letter identifying the benefits of TLTI and symptoms of tuberculosis disease; advise patient to contact you within 2 weeks (give date) or record will be closed
- If no response to letter or patient refuses treatment, close patient's record to follow-up.

K. Sample Standing Orders for Latent TB Infection

Standing Order Example: Latent TB Infection

EXAMPLE 10/09: Intended as an example for required components only, not as best practice- all standing orders should reflect individual agency protocols determined by the Medical Director.

Standing Order: Evaluation and Treatment of Latent TB Infection

Standing Order: All RNs employed or contracted by the agency who have completed orientation may use standing orders for the evaluation and treatment of latent TB infection.

Assessment:

1. Objective findings:

- The tuberculin skin test is positive (based on guidance from the NC TB Control Manual), or an interferon gamma release assay for TB is positive.
- Chest x-ray interpretation indicating no evidence of active TB disease

2. Subjective findings:

- History provided by the patient or medical record indicates:
 - a. There are no symptoms of TB, and
 - b. No sputum culture pending, and
 - c. No history of underlying liver disease, or previous reactions to INH, and
 - d. Has not received at least six months of treatment for latent TB infection in the past

Plan of Care:

1. Implementation:

- Obtain posterior-anterior (PA) view chest x-ray.
- Children under age five should also have a lateral view chest x-ray.
- Complete a Tuberculosis Epidemiological Record (DHHS 1030)
- Obtain HIV test
- For adults (> 15 years of age): Initiate Isoniazid (INH) 5 mg/kg (maximum 300 mg) daily for 9 months.
- For children (< 15 years of age): Initiate Isoniazid (INH) 10 mg/kg (maximum 300 mg) daily for 9 months.
- 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
- Prior to initiating INH, obtain baseline hepatic function panel on individuals with the following conditions based on history provided by patient or from medical record:
 - a. Average alcohol use of > 3 drinks per day
 - b. Underlying liver disease
 - c. Those persons currently taking potentially hepatotoxic drugs
- If during the course of treatment for latent TB infection, the patient complains of nausea, vomiting, loss of appetite, dark (tea or cola colored) urine, malaise, abdominal tenderness or bloating, yellow skin or sclera, instruct the patient to hold medications, draw hepatic function panel, and call physician

Conditions that require a specific treatment order for INH include:

- If baseline hepatic function panel is abnormal
- History of hepatitis or liver disease
- History of adverse reactions to INH
- Pregnant or up to 3 months postpartum

- Exposed to drug resistant case of TB
- Chest x-ray suggestive of previous TB
- HIV positive or has other immunosuppressing conditions
- If on anti-convulsive therapy
- Persons on hemodialysis
- Persons taking methotrexate

2. Nursing Action:

- Advise the patient of common adverse reactions to INH
- Advise the patient to hold medications and contact the health department if adverse reactions occur
- Ensure that physician reviews and signs all lab work results.

3. Criteria for calling the Physician:

- If baseline hepatic function panel is abnormal
- If patient complains of nausea, vomiting, loss of appetite, dark (tea or cola colored) urine, malaise, abdominal tenderness or bloating, yellow skin or sclera while taking INH

4. Follow-up Requirements:

- Evaluate the patient monthly using the Tuberculosis Flow Sheet (DHHS 2810)

Resources: NC TB Control Program Policy Manual

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: _____

Approved by: _____

Date: _____

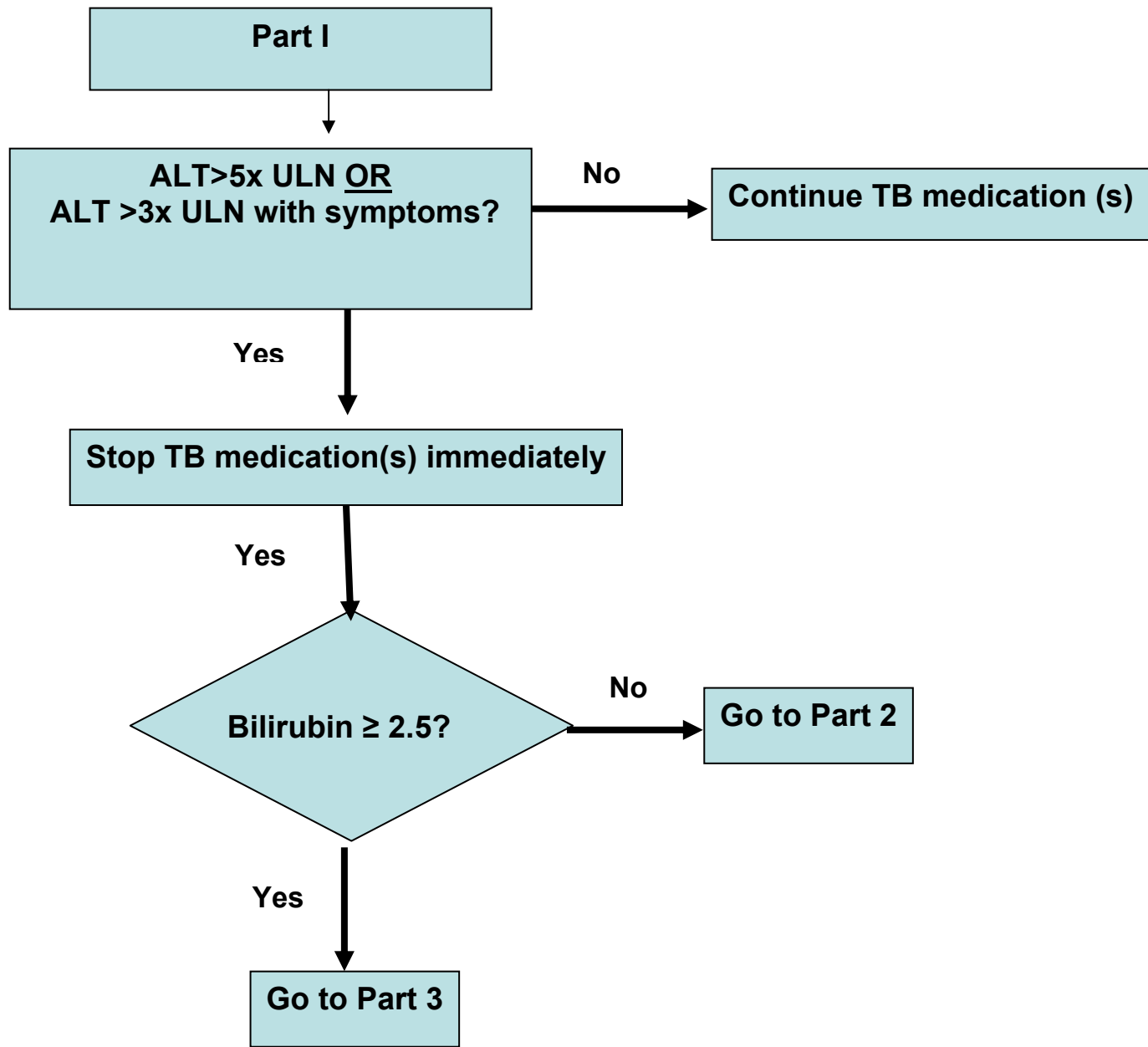
Approved by: _____

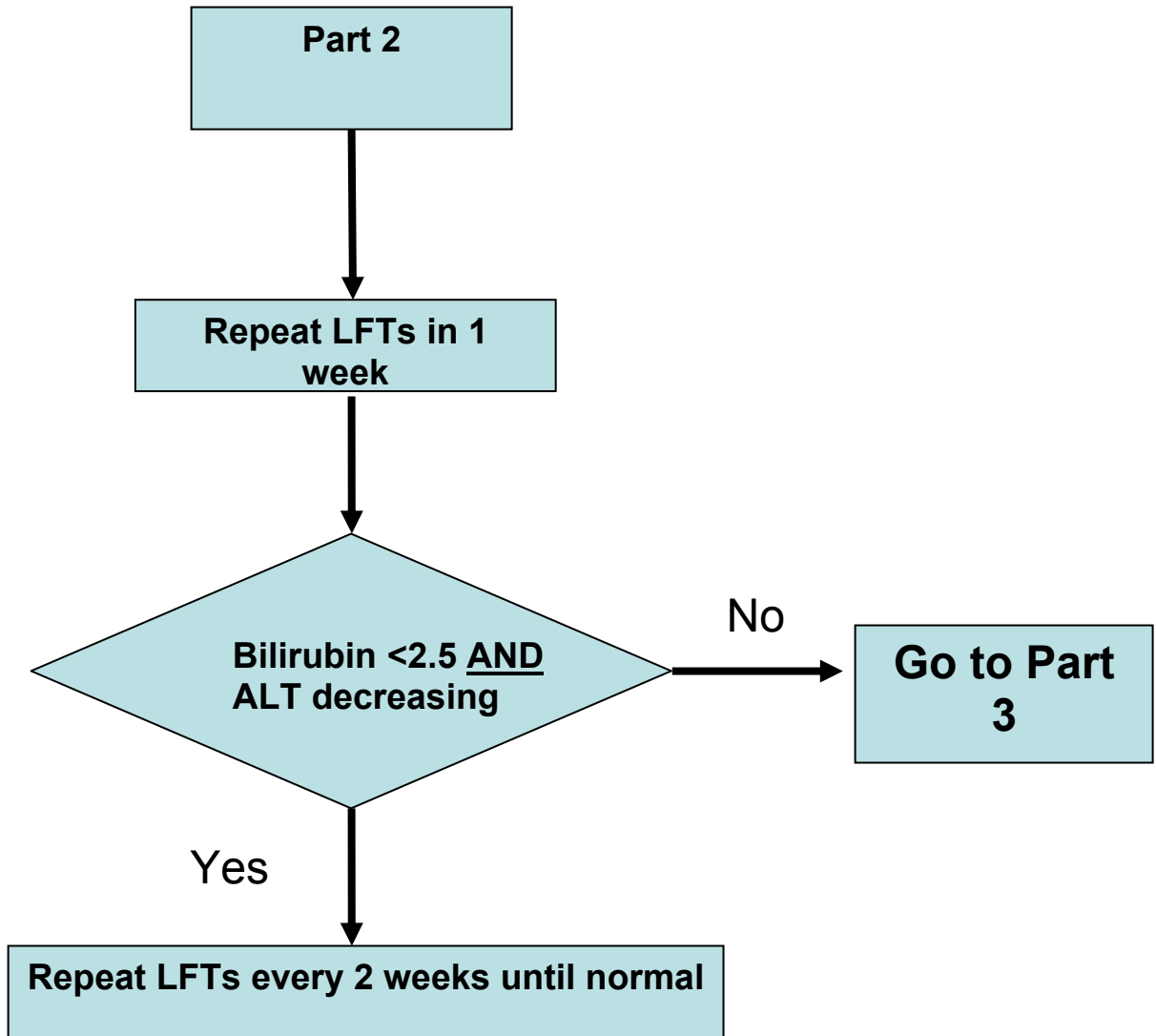
Date: _____

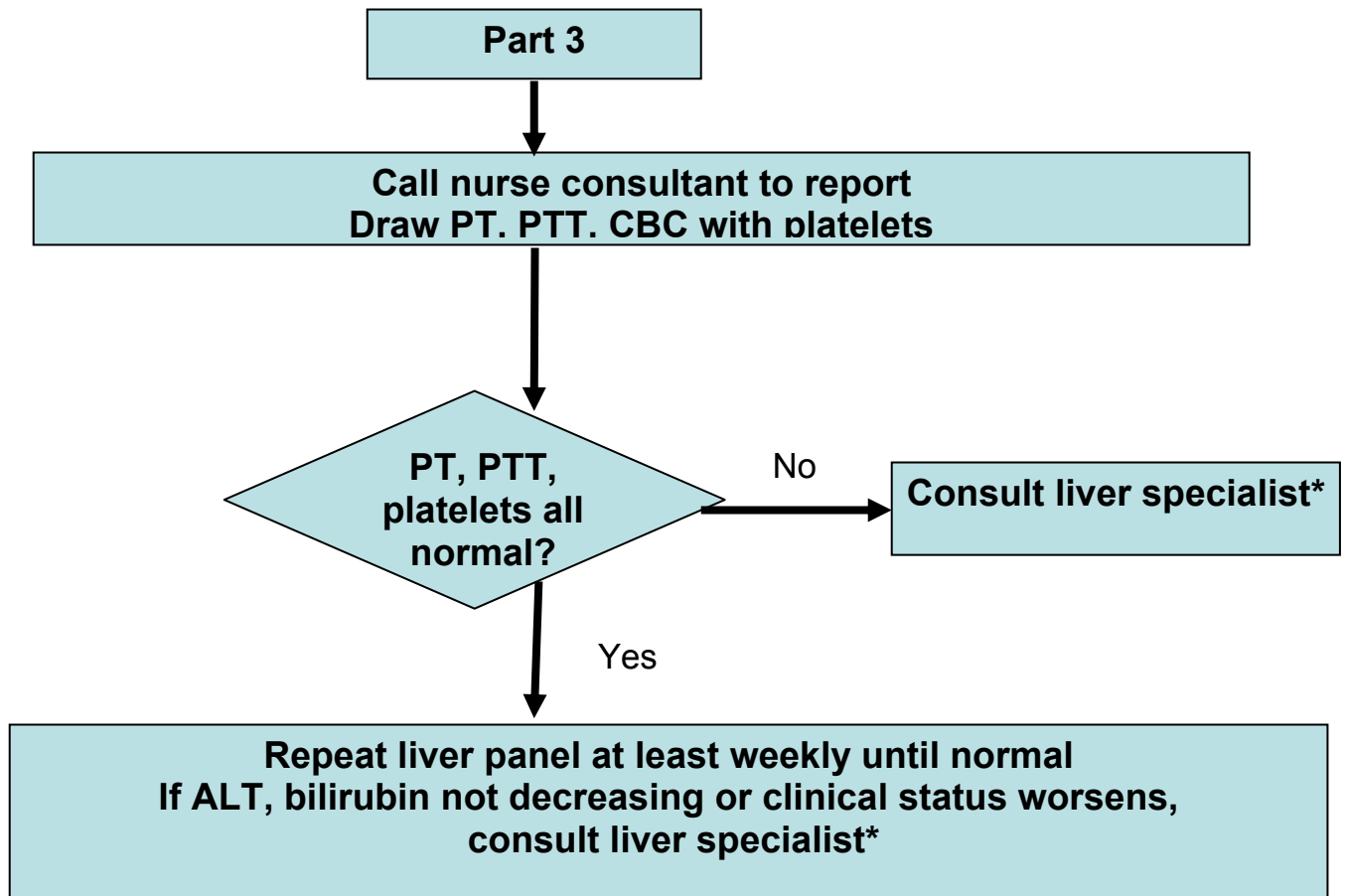
Approved by: _____

Date: _____

L. Hepatotoxicity Flowchart







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