

Service #4: Nursing Management of Persons with or Suspected to have

Mycobacterium tuberculosis Disease

(Pulmonary and/or Extrapulmonary Disease)

I. Pretreatment evaluation

- A. Perform all relevant activities under **procedure #1: Patient Assessment, Education, and Screening Procedures** (personal health history, medical screening procedures, specimen collection, tuberculosis screening procedures, referral for CXR, referral for medical evaluation (if required), patient education, signed documents, notification of relevant diagnostic testing results to patient and physician)
- B. Patients suspected of having active TB disease should have appropriate specimens collected for microscopic examination and AFB culture. When the lung is the site of disease, three sputum specimens should be obtained.
 - Prior to or at the initiation of therapy, obtain three sputum specimens, 8 to 24 hours apart, for AFB smear and culture. At least one of the samples should be collected early in the morning. **(Patients with known or suspected extrapulmonary tuberculosis should be educated about sputum collection and try to produce three sputum specimens prior to or at the initiation of therapy).** If sputum cannot be produced, consult the treating physician.
 - **Individuals with extrapulmonary TB disease should have sputum specimens submitted for AFB smear and culture, even if the CXR is normal, to exclude concomitant pulmonary disease.**
 - Susceptibility testing for INH, RIF, and EMB should be performed on a positive initial culture, regardless of the source of the specimen
- C. For all adult patients, baseline measurements of AST, ALT, bilirubin, alkaline phosphatase, serum creatinine, and complete blood count with platelet count should be obtained
- D. Testing of visual acuity (Snellen chart) and red-green color discrimination (Ishihara plates) should be obtained when EMB is to be used

II. Additional documentation required, including, but not limited to

- A. The dates and respiratory isolation status if the patient was hospitalized or in a congregate setting at diagnosis
- B. The dates of initiation of and discontinuation of home isolation by the LHD/local health authority
- C. Development of a treatment/case management plan

- D. Initiation of DOT on all cases on form **TB-206**. If DOT is not ordered, a notation of explanation in a DSHS-approved electronic reporting system, in the comments section of the **TB-400B**, or a letter from the physician is required.
- E. A review of classification within 90 days for persons reported as Class 5
- F. Nursing review monthly, medical review and prescription renewal on a TB-400B, signed by the physician, at least every 3 months or as changes in medication occur (proposed length of therapy should be documented on the physician's order)
- G. Order to Implement and Carry Out Measures for a Patient with Tuberculosis (**TB-410 or TB-410A or TB-410B**)
- The health authority should sign the control order prior to the time that the nurse explains what the order requires the patient to do. A facsimile copy, photocopy or electronic image of the health authority's signature is acceptable.
 - The nurse should document on the control order the date that the patient receives the order
 - The control order should be in the preferred language of the patient or the nurse should document that an interpreter was used
 - The patient should sign that they understand the order and acknowledge receipt. If the patient refuses to sign the control order, the nurse should document the refusal on the order and in the medical record progress notes.
 - The patient should be given a copy of the control order and the original should be placed in the patient's medical record

III. Bacteriology

- A. Prior to or at the initiation of therapy, obtain three sputum specimens, 8 to 24 hours apart, for AFB smear and culture. At least one of the samples should be collected early in the morning. **(Patients with known or suspected extrapulmonary tuberculosis should be educated about sputum collection and try to produce three sputum specimens prior to or at the initiation of therapy)**. If sputum cannot be produced, consult the treating physician.
- B. Nucleic Acid Amplification Testing should be performed on at least one respiratory specimen from each patient with signs and symptoms of pulmonary TB for whom a diagnosis of TB is being considered but has not yet been established, and for whom the test result would alter case management or TB control activities (MMWR 2009; 58:01; 7-10)
- C. For patients who had positive AFB smears at the time of diagnosis, follow-up smears may be obtained during treatment at two-week intervals until **three** consecutive specimens are negative on AFB smear. This may be useful to assess the early response to treatment and to provide an indication of infectiousness.

- D. During treatment of patients with pulmonary TB, a sputum specimen for microscopic examination and culture should be obtained at a minimum of monthly intervals until two consecutive specimens are negative on culture. **Monthly sputum samples must be collected from patients with isolates resistant to both isoniazid and rifampin (MDR-TB) throughout the treatment course.**
- E. Ideally, one of every three sputum specimens collected should be supervised, but at a minimum:
- one initial specimen at start of therapy
 - one at two months of therapy
 - one to document conversion of sputum
 - if a specimen is returned as insufficient amount or contaminated
- F. Drug susceptibility tests should be repeated on isolates from patients who have positive cultures after 3 months of treatment
- G. Results of specimens exhibiting M.TB complex cultured in laboratories other than DSHS, must be reported to the local health authority. Part of the initial isolate should be submitted to the DSHS lab in Austin for genotyping. If the specimen is positive for MDR-TB or XDR-TB, a consult must be obtained from a DSHS-recognized expert TB physician.
- H. Obtain consultation from a DSHS-recognized expert TB physician within three days of laboratory notification for all TB cases whose TB organisms are resistant to isoniazid and/or rifampin or shows a resistance to any drug on the drug susceptibility panel in accordance with policy **TB 4002**. Written documentation that 1. the consultation occurred and 2. the consultant's recommendations were followed shall be maintained in the patient's record and a copy of the consult must be sent to the DSHS Tuberculosis Services Branch within twenty-four hours. If deviations from the recommendations of the DSHS-recognized expert TB physician occur, the treating physician must consult with the DSHS-recognized expert TB physician and a justification of the deviation must be maintained in the patient's record and a copy of the justification must be sent to the DSHS Tuberculosis Services Branch within twenty-four hours.
- I. Patients should have at least one final sputum collection for culture at completion of therapy, if possible
- J. Collect additional follow-up sputum specimens during and after treatment as requested by the treating physician
- K. Collect specimens for extrapulmonary tuberculosis as requested by the treating physician

IV. **Chest X-ray**

- A. It is recommended that children less than 5 years of age and preferred that older children and adolescents up to age 18 have both posterior-anterior and lateral views; all others should have

at least posterior-anterior views. Other views or additional studies should be done only by order of the treating physician.

- B. Initial CXR should be obtained at initiation of treatment. Patients with suspected or known extrapulmonary tuberculosis should also receive a CXR to assess for pulmonary tuberculosis.
- C. In patients with negative initial cultures, a CXR is necessary after 2 months of treatment for comparison with the initial CXR
- D. If the patient is culture positive at diagnosis, a repeat CXR at completion of 2 months of treatment may be useful but is not essential. This should be done at the discretion of the treating physician.
- E. A CXR at completion of treatment is desirable as it provides a baseline for comparison with any future films, but is not essential
- F. Pregnant women should be counseled to have the abdomen appropriately shielded during CXR

V. **Special considerations** for treatment of TB disease apply to the following populations:

- A. **HIV infection:** recommendations for the treatment of TB disease are, with few exceptions, the same as those for HIV-uninfected adults. Due to the potential for drug interactions between antiretrovirals and anti-TB medications, as well as the risk of a paradoxical reaction to TB treatment (immune reconstitution syndrome), it is strongly encouraged that experts in the treatment of HIV-related TB be consulted.

Exceptions:

- INH-RPT once weekly continuation phase (Regimens 1c and 2b in Table 2 below) is contraindicated in HIV-infected patients because of an unacceptably high rate of relapse
- Patients with CD4 cell counts <100 should receive daily or three times weekly treatment (Regimen 1/1a or 3/3a). The development of acquired rifampin resistance has been noted among HIV-infected patients with advanced immunosuppression treated with twice weekly RIF or rifabutin-based regimens.

- B. **Children:** because of the high risk of disseminated TB in infants and children younger than 4 years of age, treatment should be started as soon as the diagnosis of TB is suspected. In general, the regimens recommended for adults are also the regimens of choice for infants, children, and adolescents with TB.

Note: Because it is difficult to isolate *M. tuberculosis* from a child with pulmonary TB, it is frequently necessary to rely on the results of drug susceptibility testing of the organisms isolated from the presumed source case to guide the choice of medications for the child. In cases of suspected drug-resistant TB in a child or when a source case isolate is not available, consult with a DSHS-recognized expert TB physician.

Exceptions:

- Three times weekly therapy is not recommended for children
- EMB is not used routinely in children. When clinical or epidemiologic circumstances suggest an increased probability of INH resistance, EMB can be used safely at a dose of 15-20mg/kg per day, even in children too young for routine eye testing.

TABLE 6. Epidemiological circumstances in which an exposed person is at increased risk of infection with drug-resistant *Mycobacterium tuberculosis**

- Exposure to a person who has known drug-resistant tuberculosis
- Exposure to a person with active tuberculosis who has had prior treatment for tuberculosis (treatment failure or relapse) and whose susceptibility test results are not known
- Exposure to persons with active tuberculosis from areas in which there is a high prevalence of drug resistance
- Exposure to persons who continue to have positive sputum smears after 2 months of combination chemotherapy
- Travel in an area of high prevalence of drug resistance

* This information is to be used in deciding whether or not to add a fourth drug (usually EMB) for children with active tuberculosis, not to infer the empiric need for a second-line treatment regimen.

- For disseminated TB and TB meningitis, 9-12 months of treatment is recommended

C. Extrapulmonary TB: 6 month course of therapy is recommended for treating Tb involving any site

Exceptions:

- Meningitis: 9-12 months of treatment is recommended
- Prolongation of therapy should also be considered for patients with TB in any site that is slow to respond

Note: the addition of corticosteroids is recommended for patients with TB pericarditis and TB meningitis. Consult the treating physician.

TABLE 13. Evidence-based* guidelines for the treatment of extrapulmonary tuberculosis and adjunctive use of corticosteroids†

Site	Length of therapy (mo)	Rating (duration)	Corticosteroids‡	Rating (corticosteroids)
Lymph node	6	AI	Not recommended	DIII
Bone and joint	6–9	AI	Not recommended	DIII
Pleural disease	6	AII	Not recommended	DI
Pericarditis	6	AII	Strongly recommended	AI
CNS tuberculosis including meningitis	9–12	BII	Strongly recommended	AI
Disseminated disease	6	AII	Not recommended	DIII
Genitourinary	6	AII	Not recommended	DIII
Peritoneal	6	AII	Not recommended	DIII

* For rating system, see Table 1.

† Duration of therapy for extrapulmonary tuberculosis caused by drug-resistant organisms is not known.

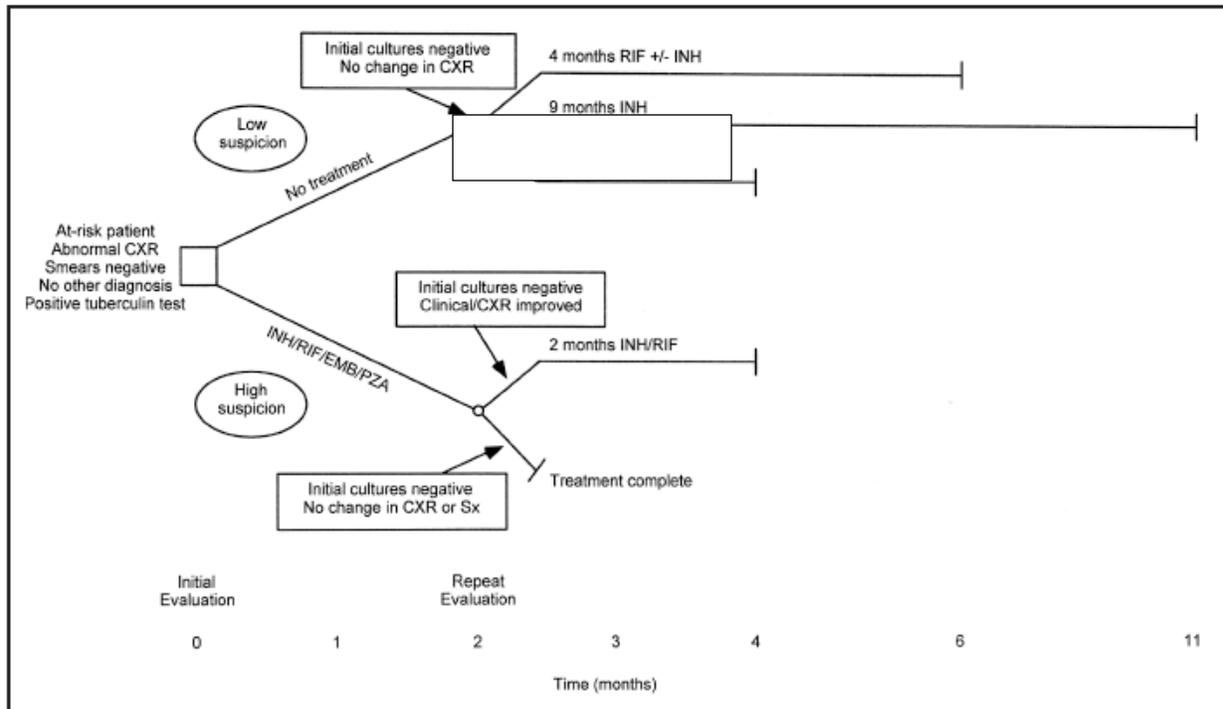
‡ Corticosteroid preparations vary among studies. See Section 8.3 for specific recommendations.

D. Culture-negative pulmonary TB and radiographic evidence of prior pulmonary TB: a diagnosis of TB can be strongly inferred by the clinical and radiographic response to anti-TB treatment

- HIV-infected patients with culture-negative pulmonary TB should be treated for a minimum of 6 months. Consult a DSHS-recognized expert TB physician.

- For radiographic evidence of prior pulmonary TB, see procedure #2: Nursing Management of Persons Infected with *Mycobacterium tuberculosis* (LTBI) or Contacts Requiring Window Prophylaxis

FIGURE 2. Treatment algorithm for active, culture-negative pulmonary tuberculosis and inactive tuberculosis



The decision to begin treatment for a patient with sputum smears that are negative depends on the degree of suspicion that the patient has tuberculosis. The considerations in choosing among the treatment options are discussed in text. If the clinical suspicion is high (bottom), then multidrug therapy should be initiated before acid-fast smear and culture results are known. If the diagnosis is confirmed by a positive culture, treatment can be continued to complete a standard course of therapy (see Figure 1). If initial cultures remain negative and treatment has consisted of multiple drugs for 2 months, then there are two options depending on repeat evaluation at 2 months (bottom): 1) if the patient demonstrates symptomatic or radiographic improvement without another apparent diagnosis, then a diagnosis of culture-negative tuberculosis can be inferred. Treatment should be continued with isoniazid and rifampin alone for an additional 2 months; 2) if the patient demonstrates neither symptomatic nor radiographic improvement, then prior tuberculosis is unlikely and treatment is complete once treatment including at least 2 months of rifampin and pyrazinamide has been administered. In low-suspicion patients not initially receiving treatment (top), if cultures remain negative, the patient has no symptoms, and the chest radiograph is unchanged at 2–3 months, there are three treatment options: these are 1) isoniazid for 9 months, 2) rifampin with or without isoniazid for 4 months, or 3) rifampin and pyrazinamide for 2 months. CXR = chest X-ray; EMB = ethambutol; INH = isoniazid; PZA = pyrazinamide; RIF = rifampin; Sx = signs/symptoms. (It should be noted that the RIF/PZA 2-month regimen should be used only for patients who are not likely to complete a longer course of treatment and can be monitored closely.)

- E. **Renal insufficiency and end-stage renal disease:** specific dosing guidelines are provided in Table 15. Confirm dosages with the treating physician before administering medications.

TABLE 15. Dosing recommendations for adult patients with reduced renal function and for adult patients receiving hemodialysis

Drug	Change in frequency?	Recommended dose and frequency for patients with creatinine clearance <30 ml/min or for patients receiving hemodialysis
Isoniazid	No change	300 mg once daily, or 900 mg three times per week
Rifampin	No change	600 mg once daily, or 600 mg three times per week
Pyrazinamide	Yes	25–35 mg/kg per dose three times per week (not daily)
Ethambutol	Yes	15–25 mg/kg per dose three times per week (not daily)
Levofloxacin	Yes	750–1,000 mg per dose three times per week (not daily)
Cycloserine	Yes	250 mg once daily, or 500 mg/dose three times per week*
Ethionamide	No change	250-500 mg/dose daily
<i>p</i> -Aminosalicylic acid	No change	4 g/dose, twice daily
Streptomycin	Yes	12–15 mg/kg per dose two or three times per week (not daily)
Capreomycin	Yes	12–15 mg/kg per dose two or three times per week (not daily)
Kanamycin	Yes	12–15 mg/kg per dose two or three times per week (not daily)
Amikacin	Yes	12–15 mg/kg per dose two or three times per week (not daily)

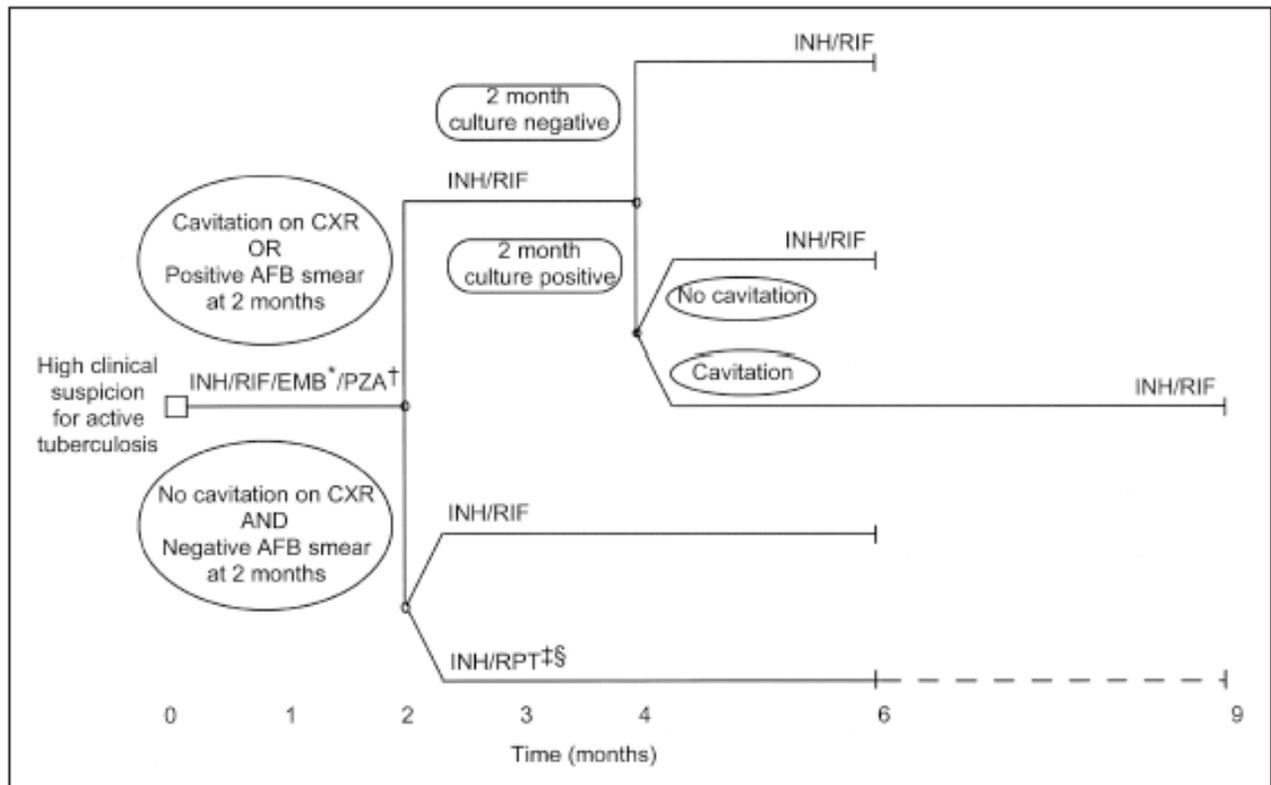
Standard doses are given unless there is intolerance. The medications should be given after hemodialysis on the day of hemodialysis. Monitoring of serum drug concentrations should be considered to ensure adequate drug absorption, without excessive accumulation, and to assist in avoiding toxicity. Data currently are not available for patients receiving peritoneal dialysis. Until data become available, begin with doses recommended for patients receiving hemodialysis and verify adequacy of dosing, using serum concentration monitoring. * The appropriateness of 250-mg daily doses has not been established. There should be careful monitoring for evidence of neurotoxicity (see Section 3).

- F. **Liver disease:** INH, RIF, and PZA can all cause hepatitis that may result in additional liver damage in patients with preexisting liver disease. However, because of the effectiveness of these drugs, they should be used if at all possible. Consult the treating physician or a DSHS-recognized expert TB physician if significant concerns exist.
- G. **Pregnancy and breastfeeding:** because of the risk of TB to the fetus, treatment of TB in pregnant women should be initiated whenever the probability of maternal disease is moderate to high. Breastfeeding should not be discouraged for women being treated with the first-line anti-TB medications because the small concentrations of these drugs in breast milk do not produce toxicity in the nursing newborn. Consult the treating physician or a DSHS-recognized expert TB physician if significant concerns exist.

VI. Treatment of active TB disease

- A. On the basis of substantial clinical experience, 5 day-a-week drug administration by DOT is considered to be equivalent to 7 day-a-week administration; thus, either may be considered “daily”.
- B. If PZA cannot be included in the initial regimen, or if the isolate is determined to be resistant to PZA, a regimen consisting of INH, RIF, and EMB should be given for the initial 2 months (Regimen4) followed by INH and RIF for 7 months given either daily or twice weekly (Regimens 4a and 4b). Minimum duration of therapy is a total of 9 months.
- C. If RIF cannot be included in the initial regimen, minimum duration of treatment is a total of 12-18 months. The actual regimen used will be determined by consultation with a DSHS-recognized expert TB physician.
- D. Patients who have cavitation on initial CXR and who have positive culture at completion of 2 months of therapy are at substantially increased risk of relapse. For these patients it is recommended that the continuation phase of treatment be prolonged to 7 months, making a total treatment period of 9 months.
- E. Patients with noncavitary pulmonary TB and a negative AFB smear at 2 months who are started on the once weekly RPT-INH continuation phase and are subsequently found to be culture positive at 2 months should have treatment extended by an additional 3 months for a total of 9 months

FIGURE 1. Treatment algorithm for tuberculosis.



Patients in whom tuberculosis is proved or strongly suspected should have treatment initiated with isoniazid, rifampin, pyrazinamide, and ethambutol for the initial 2 months. A repeat smear and culture should be performed when 2 months of treatment has been completed. If cavities were seen on the initial chest radiograph or the acid-fast smear is positive at completion of 2 months of treatment, the continuation phase of treatment should consist of isoniazid and rifampin daily or twice weekly for 4 months to complete a total of 6 months of treatment. If cavitation was present on the initial chest radiograph and the culture at the time of completion of 2 months of therapy is positive, the continuation phase should be lengthened to 7 months (total of 9 months of treatment). If the patient has HIV infection and the CD4⁺ cell count is <100/ μ l, the continuation phase should consist of daily or three times weekly isoniazid and rifampin. In HIV-uninfected patients having no cavitation on chest radiograph and negative acid-fast smears at completion of 2 months of treatment, the continuation phase may consist of either once weekly isoniazid and rifampin, or daily or twice weekly isoniazid and rifampin, to complete a total of 6 months (bottom). Patients receiving isoniazid and rifampin, and whose 2-month cultures are positive, should have treatment extended by an additional 3 months (total of 9 months).

^{*} EMB may be discontinued when results of drug susceptibility testing indicate no drug resistance.

[†] PZA may be discontinued after it has been taken for 2 months (56 doses).

[‡] RPT should not be used in HIV-infected patients with tuberculosis or in patients with extrapulmonary tuberculosis.

[§] Therapy should be extended to 9 months if 2-month culture is positive.

CXR = chest radiograph; EMB = ethambutol; INH = isoniazid; PZA = pyrazinamide; RIF = rifampin; RPT = rifapentine.

TABLE 2. Drug regimens for culture-positive pulmonary tuberculosis caused by drug-susceptible organisms

Regimen	Initial phase		Continuation phase			Range of total doses (minimal duration)	Rating* (evidence) [†]	
	Drugs	Interval and doses [‡] (minimal duration)	Regimen	Drugs	Interval and doses ^{‡§} (minimal duration)		HIV ⁻	HIV ⁺
1	INH RIF PZA EMB	Seven days per week for 56 doses (8 wk) or 5 d/wk for 40 doses (8 wk) [¶]	1a	INH/RIF	Seven days per week for 126 doses (18 wk) or 5 d/wk for 90 doses (18 wk) [¶]	182–130 (26 wk)	A (I)	A (II)
			1b	INH/RIF	Twice weekly for 36 doses (18 wk)	92–76 (26 wk)	A (I)	A (II) [#]
			1c**	INH/RPT	Once weekly for 18 doses (18 wk)	74–58 (26 wk)	B (I)	E (I)
2	INH RIF PZA EMB	Seven days per week for 14 doses (2 wk), then twice weekly for 12 doses (6 wk) or 5 d/wk for 10 doses (2 wk), [¶] then twice weekly for 12 doses (6 wk)	2a	INH/RIF	Twice weekly for 36 doses (18 wk)	62–58 (26 wk)	A (II)	B (II) [#]
			2b**	INH/RPT	Once weekly for 18 doses (18 wk)	44–40 (26 wk)	B (I)	E (I)
3	INH RIF PZA EMB	Three times weekly for 24 doses (8 wk)	3a	INH/RIF	Three times weekly for 54 doses (18 wk)	78 (26 wk)	B (I)	B (II)
4	INH RIF EMB	Seven days per week for 56 doses (8 wk) or 5 d/wk for 40 doses (8 wk) [¶]	4a	INH/RIF	Seven days per week for 217 doses (31 wk) or 5 d/wk for 155 doses (31 wk) [¶]	273–195 (39 wk)	C (I)	C (II)
			4b	INH/RIF	Twice weekly for 62 doses (31 wk)	118–102 (39 wk)	C (I)	C (II)

Definition of abbreviations: EMB = Ethambutol; INH = isoniazid; PZA = pyrazinamide; RIF = rifampin; RPT = rifapentine.

* Definitions of evidence ratings: A = preferred; B = acceptable alternative; C = offer when A and B cannot be given; E = should never be given.

[†] Definition of evidence ratings: I = randomized clinical trial; II = data from clinical trials that were not randomized or were conducted in other populations; III = expert opinion.

[‡] When DOT is used, drugs may be given 5 days/week and the necessary number of doses adjusted accordingly. Although there are no studies that compare five with seven daily doses, extensive experience indicates this would be an effective practice.

[§] Patients with cavitation on initial chest radiograph and positive cultures at completion of 2 months of therapy should receive a 7-month (31 week; either 217 doses [daily] or 62 doses [twice weekly]) continuation phase.

[¶] Five-day-a-week administration is always given by DOT. Rating for 5 day/week regimens is AIII.

[#] Not recommended for HIV-infected patients with CD4⁺ cell counts <100 cells/μl.

** Options 1c and 2b should be used only in HIV-negative patients who have negative sputum smears at the time of completion of 2 months of therapy and who do not have cavitation on initial chest radiograph (see text). For patients started on this regimen and found to have a positive culture from the 2-month specimen, treatment should be extended an extra 3 months.

TABLE 3. Doses* of antituberculosis drugs for adults and children†

Drug	Preparation	Adults/children	Doses			
			Daily	1x/wk	2x/wk	3x/wk
First-line drugs						
Isoniazid	Tablets (50 mg, 100 mg, 300 mg); elixir (50 mg/5 ml); aqueous solution (100 mg/ml) for intravenous or intramuscular injection	Adults (max.) Children (max.)	5 mg/kg (300 mg) 10–15 mg/kg (300 mg)	15 mg/kg (900 mg) —	15 mg/kg (900 mg) 20–30 mg/kg (900 mg)	15 mg/kg (900 mg) —
Rifampin	Capsule (150 mg, 300 mg); powder may be suspended for oral administration; aqueous solution for intravenous injection	Adults [‡] (max.) Children (max.)	10 mg/kg (600 mg) 10–20 mg/kg (600 mg)	— —	10 mg/kg (600 mg) 10–20 mg/kg (600 mg)	10 mg/kg (600 mg) —
Rifabutin	Capsule (150 mg)	Adults [‡] (max.) Children	5 mg/kg (300 mg) Appropriate dosing for children is unknown	— Appropriate dosing for children is unknown	5 mg/kg (300 mg) Appropriate dosing for children is unknown	5 mg/kg (300 mg) Appropriate dosing for children is unknown
Rifapentine	Tablet (150 mg, film coated)	Adults Children	— The drug is not approved for use in children	10 mg/kg (continuation phase) (600 mg) The drug is not approved for use in children	— The drug is not approved for use in children	— The drug is not approved for use in children
Pyrazinamide	Tablet (500 mg, scored)	Adults Children (max.)	See Table 4 15–30 mg/kg (2.0 g)	— —	See Table 4 50 mg/kg (2 g)	See Table 4 —
Ethambutol	Tablet (100 mg, 400 mg)	Adults Children [§] (max.)	See Table 5 15–20 mg/kg daily (1.0 g)	— —	See Table 5 50 mg/kg (2.5 g)	See Table 5 —
Second-line drugs						
Cycloserine	Capsule (250 mg)	Adults (max.) Children (max.)	10–15 mg/kg/d (1.0 g in two doses), usually 500–750 mg/d in two doses [¶] 10–15 mg/kg/d (1.0 g/d)	There are no data to support intermittent administration —	There are no data to support intermittent administration —	There are no data to support intermittent administration —
Ethionamide	Tablet (250 mg)	Adults [¶] (max.) Children (max.)	15–20 mg/kg/d (1.0 g/d), usually 500–750 mg/d in a single daily dose or two divided doses [¶] 15–20 mg/kg/d (1.0 g/d)	There are no data to support intermittent administration There are no data to support intermittent administration	There are no data to support intermittent administration There are no data to support intermittent administration	There are no data to support intermittent administration There are no data to support intermittent administration
Streptomycin	Aqueous solution (1-g vials) for intravenous or intramuscular administration	Adults (max.) Children (max.)	** 20–40 mg/kg/d (1 g)	** —	** 20 mg/kg	** —
Amikacin/ kanamycin	Aqueous solution (500-mg and 1-g vials) for intravenous or intramuscular administration	Adults (max.) Children (max.)	** 15–30 mg/kg/d (1 g) intravenous or intramuscular as a single daily dose	** —	** 15–30 mg/kg	** —
Capreomycin	Aqueous solution (1-g vials) for intravenous or intramuscular administration	Adults (max.) Children (max.)	** 15–30 mg/kg/d (1 g) as a single daily dose	** —	** 15–30 mg/kg	** —
p-Aminosalicylic acid (PAS)	Granules (4-g packets) can be mixed with food; tablets (500 mg) are still available in some countries, but not in the United States; a solution for intravenous administration is available in Europe	Adults Children	8–12 g/d in two or three doses 200–300 mg/kg/d in two to four divided doses (10 g)	There are no data to support intermittent administration There are no data to support intermittent administration	There are no data to support intermittent administration There are no data to support intermittent administration	There are no data to support intermittent administration There are no data to support intermittent administration
Levofloxacin	Tablets (250 mg, 500 mg, 750 mg); aqueous solution (500-mg vials) for intravenous injection	Adults Children	500–1,000 mg daily ††	There are no data to support intermittent administration ††	There are no data to support intermittent administration ††	There are no data to support intermittent administration ††

TABLE 3. (Continued) Doses* of antituberculosis drugs for adults and children†

Drug	Preparation	Adults/children	Doses			
			Daily	1x/wk	2x/wk	3x/wk
Moxifloxacin	Tablets (400 mg); aqueous solution (400 mg/250 ml) for intravenous injection	Adults	400 mg daily	There are no data to support intermittent administration	There are no data to support intermittent administration	There are no data to support intermittent administration
		Children	‡	‡	‡	‡
Gatifloxacin	Tablets (400 mg); aqueous solution (200 mg/20 ml; 400 mg/40 ml) for intravenous injection	Adults	400 mg daily	There are no data to support intermittent administration	There are no data to support intermittent administration	There are no data to support intermittent administration
		Children	§§	§§	§§	§§

* Dose per weight is based on ideal body weight. Children weighing more than 40 kg should be dosed as adults.
 † For purposes of this document adult dosing begins at age 15 years.
 ‡ Dose may need to be adjusted when there is concomitant use of protease inhibitors or nonnucleoside reverse transcriptase inhibitors.
 § The drug can likely be used safely in older children but should be used with caution in children less than 5 years of age, in whom visual acuity cannot be monitored. In younger children EMB at the dose of 15 mg/kg per day can be used if there is suspected or proven resistance to INH or RIF.
 ¶ It should be noted that, although this is the dose recommended generally, most clinicians with experience using cycloserine indicate that it is unusual for patients to be able to tolerate this amount. Serum concentration measurements are often useful in determining the optimal dose for a given patient.
 # The single daily dose can be given at bedtime or with the main meal.
 ** Dose: 15 mg/kg per day (1 g), and 10 mg/kg in persons more than 59 years of age (750 mg). Usual dose: 750–1,000 mg administered intramuscularly or intravenously, given as a single dose 5–7 days/week and reduced to two or three times per week after the first 2–4 months or after culture conversion, depending on the efficacy of the other drugs in the regimen.
 †† The long-term (more than several weeks) use of levofloxacin in children and adolescents has not been approved because of concerns about effects on bone and cartilage growth. However, most experts agree that the drug should be considered for children with tuberculosis caused by organisms resistant to both INH and RIF. The optimal dose is not known.
 †‡ The long-term (more than several weeks) use of moxifloxacin in children and adolescents has not been approved because of concerns about effects on bone and cartilage growth. The optimal dose is not known.
 §§ The long-term (more than several weeks) use of gatifloxacin in children and adolescents has not been approved because of concerns about effects on bone and cartilage growth. The optimal dose is not known.

TABLE 4. Suggested pyrazinamide doses, using whole tablets, for adults weighing 40–90 kilograms

	Weight (kg)*		
	40–55	56–75	76–90
Daily, mg (mg/kg)	1,000 (18.2–25.0)	1,500 (20.0–26.8)	2,000† (22.2–26.3)
Thrice weekly, mg (mg/kg)	1,500 (27.3–37.5)	2,500 (33.3–44.6)	3,000† (33.3–39.5)
Twice weekly, mg (mg/kg)	2,000 (36.4–50.0)	3,000 (40.0–53.6)	4,000† (44.4–52.6)

* Based on estimated lean body weight.
 † Maximum dose regardless of weight.

TABLE 5. Suggested ethambutol doses, using whole tablets, for adults weighing 40–90 kilograms

	Weight (kg)*		
	40–55	56–75	76–90
Daily, mg (mg/kg)	800 (14.5–20.0)	1,200 (16.0–21.4)	1,600† (17.8–21.1)
Thrice weekly, mg (mg/kg)	1,200 (21.8–30.0)	2,000 (26.7–35.7)	2,400† (26.7–31.6)
Twice weekly, mg (mg/kg)	2,000 (36.4–50.0)	2,800 (37.3–50.0)	4,000† (44.4–52.6)

* Based on estimated lean body weight.
 † Maximum dose regardless of weight.

VII. If treatment for TB disease is recommended

- A. There must be an appropriate **physician order** on record including name of drug(s), dosage, frequency, route and method of administration (directly observed therapy or self-administered therapy), length of treatment, and maximum number of refills:
- Written order on **TB-400B**, or
 - Written order on a prescription form or physician letterhead, or
 - Verbal order documented in the progress notes
 - All prescriptions and verbal orders must be followed by form TB-400B with the treating physician’s signature faxed or mailed within 96 hours

- B. Patient should receive an **initial clinical evaluation and follow-up clinical evaluations** at least monthly with clinical assessment for tuberculosis disease medication toxicity, in the preferred language of the patient or using an interpreter, recorded on form **TB-205**
- This evaluation should include questioning about side effects and a brief physical assessment checking for signs of hepatitis
 - For female patients of childbearing potential: counsel the patient that rifamycins may make hormonal contraceptive methods less effective, encourage the patient to add a back-up barrier method to prevent pregnancy, and emphasize the importance of avoiding pregnancy while on treatment and, for rifapentine, up to two weeks after stopping the medicine
 - Patients should be educated about the symptoms and signs that could be side effects associated with treatment of TB disease and advised to stop treatment and promptly seek medical evaluation when they occur, including: unexplained anorexia, nausea, vomiting, dark urine, icterus, rash, persistent paresthesias of the hands and feet, persistent fatigue, weakness or fever lasting 3 or more days, abdominal tenderness, easy bruising or bleeding, and arthralgia
 - At each monthly visit, patients **taking EMB** should be questioned regarding possible visual disturbances including blurred vision or scotomata and undergo visual acuity (Snellen chart) and color discrimination (Ishihara plates)
 - Patients on rifabutin should receive vision screening using the Snellen chart monthly
 - If AST levels exceed more than 5 times the upper limit of normal (with or without symptoms) or more than 3 times normal in the presence of symptoms, hepatotoxic drugs should be stopped immediately and the patient evaluated carefully. Similarly, a significant increase in bilirubin and/or alkaline phosphatase is cause for a prompt evaluation. Serologic testing for Hepatitis A, B, and C should be performed and the patient questioned carefully regarding symptoms suggestive of biliary tract disease and exposures to other potential hepatotoxins, particularly alcohol and hepatotoxic medications. Consult the treating physician for orders for how to re-initiate the medications.
 - Serious adverse reactions that result in hospitalization or death should be reported to the DSHS TB/HIV/STD Unit within two working days on form **EF 12-12274**. Contact the DSHS TB nurse consultant for instructions, if needed. Adverse reactions resulting in hospitalization or death should also be reported to the CDC Division of Tuberculosis Elimination at 404-639-8401 or LTBIldrugevents@cdc.gov
 - Adverse events or medication errors should be reported to the DSHS TB/HIV/STD Unit within five working days on form **EF 12-12274**. Contact the DSHS TB nurse consultant for instructions, if needed. Adverse events should also be reported to FDA MedWatch at <http://www.fda.gov/medwatch>, by submitting a MedWatch Form 3500 (available at http://www.fds.gov/medwatch/safety/FDA-3500_fillable.pdf) or by calling 1-800-FDA-1088.
- C. Patients receiving rifamycins should be counseled about the side effects of rifampin, rifapentine, and rifabutin:

- Hepatotoxicity, evidenced by transient asymptomatic hyperbilirubinemia, may occur in 0.6% of persons taking RIF. Hepatitis is more likely when RIF is combined with INH.
- Cutaneous reactions, such as pruritus (with or without a rash), may occur in 6% of persons taking RIF. They are generally self-limited and may not be a true hypersensitivity; continued treatment may be possible. Consult the treating physician if this occurs.
- Rarely, rifamycins can be associated with hypersensitivity reactions, including hypotension, nephritis or thrombocytopenia, and manifested by symptoms such as fever, headache, dizziness/lightheadedness, musculoskeletal pain, petechiae, and pruritus.
- Gastrointestinal symptoms such as nausea, anorexia, and abdominal pain are rarely severe enough to discontinue treatment.
- Orange discoloration of body fluids is expected and harmless, but patients should be advised beforehand. Soft contact lenses and dentures may be permanently stained.
- RIF and RPT interact with a number of drugs, causing drug-drug interactions. They are known to reduce concentrations of methadone, warfarin, hormonal contraceptives, and phenytoin. Women using hormonal contraceptives should be advised to consider an alternative method of contraception (e.g., a barrier method).
- RIF is contraindicated, or should be used with caution, in HIV-infected individuals being treated with certain antiretroviral medications. Substitution of rifabutin for RIF in the 4-month regimen may be considered for such patients. RPT should not be used in HIV-infected persons taking antiretroviral therapy.

VIII. Directly observed therapy (DOT)

- All regimens should be given only under DOT
- For patients receiving DOT, in the event of evacuation,
 - Re-establish contact, as soon as possible. Confirm location and reinstitute DOT or transfer to new jurisdiction for continuation of treatment.
 - For TB smear positive cases and suspects, ensure appropriate transportation and placement in coordination with DSHS Central Office
- Document doses of medications given by DOT on form **TB-206**

IX. Laboratory testing

- For all adult patients, **baseline measurements** of AST, ALT, bilirubin, alkaline phosphatase, serum creatinine, and complete blood count with platelet count should be obtained
- Routine laboratory monitoring of hepatic and renal function and platelet count during treatment** is indicated for
 - persons whose baseline tests are abnormal

- other persons at risk for hepatotoxicity (history of liver disease, HIV infection, HBV, HCV or other chronic hepatitis, sexual or household contact with individuals chronically infected with viral hepatitis, chronic hemodialysis, receipt of clotting factors prior to 1987, pregnant or less than 3 months post-partum, jaundice, substance abuse, taking other potentially hepatotoxic medications, other chronic medical conditions such as DM, CHF, or chronic kidney disease)
- or as ordered by the treating physician

C. Laboratory testing may also be indicated for the evaluation of possible adverse effects that occur during the course of treatment, as ordered by the treating physician

- Obtain liver function studies on the same day, if possible
- Do not restart medication without a physician's order

X. Other treatment notes

A. Schedule the patient for medical reviews with a physician at least every three months or as indicated for the following:

- Assessment of patient clinical status
- Drug prescription renewal or adjustments in treatment regimen
- Other orders as indicated

If resources allow, patients should see a physician in a face-to-face encounter at the time of initiation of therapy and every month, for clinical assessment

B. At the first sign of non-compliance or questionable compliance, discuss with the treating physician for consideration of initiating court-ordered management

C. Generally patients do not require follow-up after completion of therapy but should be instructed to seek care promptly if signs or symptoms recur

D. Refer patients for other medical and social services as appropriate

XI. When INH is used , **pyridoxine supplementation** should be given to the following :

- Pregnant women
- Breastfeeding infants
- Patients with diets likely to be deficient in pyridoxine

D. Patients who are at risk for developing paresthesias (such as HIV/AIDS, alcohol use, diabetes mellitus)

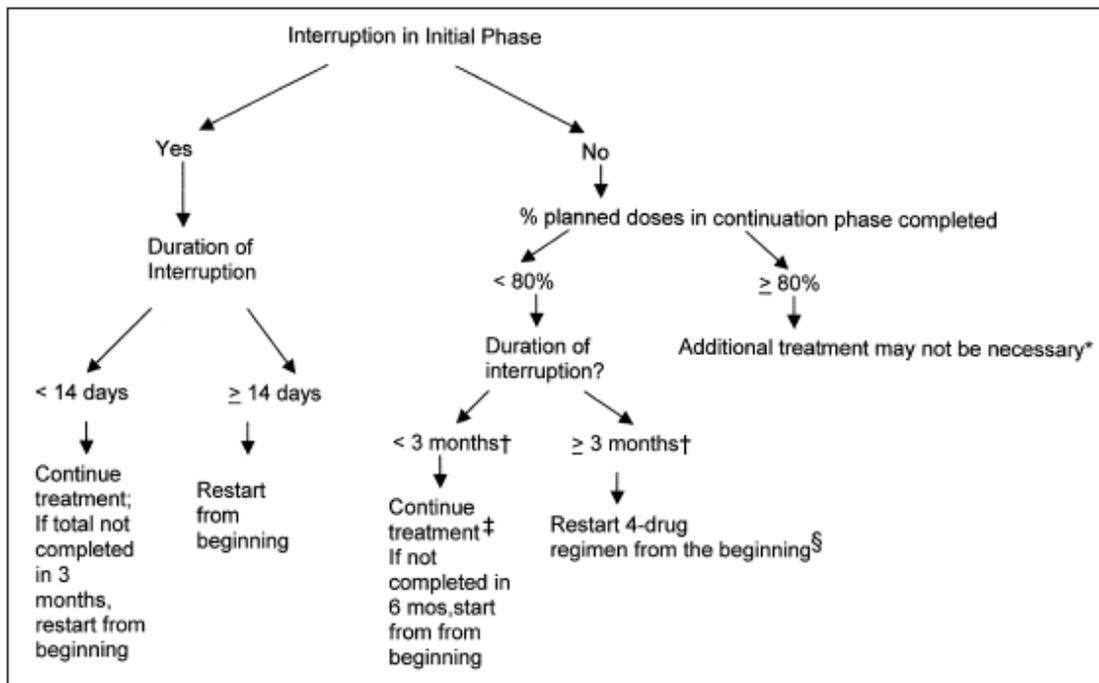
E. Patients who experience paresthesias while taking INH

XII. Completion of therapy: see Table 2 under VI. Treatment of active TB disease

Note: in some cases, either because of drug toxicity or nonadherence to the regimen, the specified number of doses cannot be administered within the targeted time period. In such cases, it is recommended that all of the specified number of doses for the initial phase be delivered within 3 months and those for the 4-month continuation phase be delivered within 6 months, so that the 6-month regimen should be completed within 9 months.

XIII. Interruption of therapy: When interruptions occur, consult with the treating physician to decide whether to restart a complete course of treatment or simply to continue as intended originally

FIGURE 5. Management of treatment interruptions



* Patients who were initially AFB smear-positive should receive additional therapy.
 † Recheck smears and cultures (if positive, check drug susceptibility results). Start DOT if not already being used.
 ‡ If repeat culture is positive, restart four-drug regimen while waiting for drug susceptibility results. If repeat culture is negative, continue therapy to complete regimen within 9 months of original start date.
 § If repeat culture is positive, continue four-drug regimen while waiting for drug susceptibility results. If repeat culture is negative, consider stopping therapy if patient has received a total of 9 months of therapy.

XIV. Consults

- A. A consult with a DSHS-recognized expert TB physician must be requested on all cases where susceptibility studies indicate resistance to isoniazid and/or rifampin. These patients are at high risk for treatment failure and further acquired drug resistance.
- B. A DSHS-recognized expert TB physician consult should also be requested on patients who remain symptomatic or whose smears/cultures remain positive after 2 months of appropriate therapy
- C. Consultations on pediatric cases are encouraged but are left to the discretion of the treating physician
- D. Patients with HIV infection and TB should be strongly encouraged to obtain care from a provider who is knowledgeable in treatment of HIV. Treatment of TB and HIV should be coordinated.
- E. If treatment is interrupted for more than 2 weeks in the initiation phase of therapy or for more than 2 months in the continuation phase of therapy, consultation with the treating physician and/or a DSHS-recognized expert TB physician should be considered before restarting therapy. Repeat cultures should also be performed. The patient must be evaluated by the treating physician before restarting therapy.
- F. Treatment failure is defined as continued or recurrently positive cultures during the course of anti-TB therapy. Patients whose sputum cultures remain positive after 4 months of treatment should be deemed treatment failures and consultation with a DSHS-recognized expert TB physician must occur.