Treatment and Management of Tuberculosis Disease

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Suspect TB in patients with these symptoms:

- Prolonged productive cough that lasts three weeks or longer
- Fever
- Night sweats
- Weight loss
- Hemoptysis (coughing up blood)
- Fatigue
- Loss of appetite
- Unexplained weight loss
- Chest pain

Especially if the individual:

- was identified as a contact to an infectious TB patient
- was born in or traveled to a country where TB is common
- is a resident or employee of a high-risk congregate setting (i.e. long term care facilities, correctional facilities, homeless shelters)
- is living with HIV, is immunosuppressed, or has other medical risk factors that increase the likelihood of progression to TB disease if infected (end stage renal disease, diabetes, taking TNF-α antagonists, etc.)
- has a history of substance abuse of any kind
- has a positive Interferon-gamma release assay (IGRA) or tuberculin skin test (TST)

Pre-treatment Screening procedures:

- All suspected and confirmed cases of TB disease are reportable within one working day. If TB disease is suspected, report the patient to the LHD. Consult with the IDOH regional nurse consultant or TB expert if needed.
- Obtain a posterior-anterior & lateral chest x-ray
- Draw blood for an IGRA or place and read a tuberculin skin test if not already done
- If pulmonary symptoms and/or abnormal chest x-ray, obtain 3 consecutive sputum specimens 8-24 hours apart (at least one early morning specimen) for acid-fast bacilli smear, nucleic acid amplification test (NAAT), culture, molecular and drug-based susceptibility and genotype testing
- Test visual acuity and red-green color discrimination for those who will be taking ethambutol
- Obtain a baseline EKG for those that will be taking the RPT-MOX regimen
- Lab work: Liver function tests, CBC w/platelets, serum uric acid, BUN, and creatinine
- Perform HIV testing for all patients
- Perform serologic testing for hepatitis B and C if risk factors are present

Indiana Department of Health

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RIPE Treatment Regimen Drugs and Dosages

Drug	Daily (maximum)	Three Times per Week (maximum)*	Adverse Reactions
Isoniazid (INH)	Adults: 5 mg/kg (300 mg) Children†: 10-15 mg/kg (300 mg)	Adults: 15 mg/kg (900 mg) Children: not established	Hepatic enzyme elevation, hepatitis, rash, peripheral neuropathy, mild central nervous system effects, drug interactions
Rifampin (RIF)	Adults: 10 mg/kg (600 mg) Children†: 10-20 mg/kg (600 mg)	Adults: 10 mg/kg (600 mg) Children: not established	Cutaneous reactions, GI intolerance, drug interactions, hepatitis, bleeding problems, flu-like symptoms, orange discoloration of body fluids
Pyrazinamide (PZA)^	Adults: see table below Children: 35 (30-40) mg/kg Patient Weight / Suggested Dose Daily / (mg/kg)# 40-55 kg / 1000 mg / 18.2-25.0 56-75 kg / 1500 mg / 20.0-26.8 76-90 kg / 2000 mg / 22.2-26.3	Adults: see table below Children: not established Patient Weight / Suggested Dose Daily / (mg/kg)# 40-55 kg / 1500 mg / 27.3-37.5 56-75 kg / 2500 mg / 33.3-44.6 76-90 kg / 3000 mg / 33.3-39.5	GI intolerance, hepatitis, rash, joint aches, hyperuricemia, gout (rare), photosensitivity
Ethambutol (EMB)^	Adults: see table below Children: 20 (15-25) mg/kg Patient Weight / Suggested Dose Daily / (mg/kg)# 40-55 kg / 800 mg / 14.5-20.0 56-75 kg / 1200 mg / 16.0-21.4 76-90 kg / 1600 mg / 17.8-21.1	Adults: see table below Children: not established Patient Weight / Suggested Dose Daily / (mg/kg)# 40-55 kg / 1200 mg / 21.8-30.0 56-75 kg / 2000 mg / 26.7-35.7 76-90 kg / 2400 mg / 26.7-31.6	Optic neuritis

Range numbers are the calculated mg/kg doses for patients at the highest and lowest weights in the weight band.
^With normal renal function
* Three times per week dosing is not used often and is reserved for certain circumstances. Please consult with a regional nurse consultant/TB expert.
† Consult as needed to determine if pediatric or adult dosing is needed.

RIPE Treatment Regimen Alternative Drugs and Dosages

Drug	Daily (maximum)	Three Times per Week (maximum)*	Adverse Reactions
Rifapentine (RPT)	Adults: 10 mg/kg (600 mg) Children: Tuberculosis disease: for children greater than or equal to 12 years of age, same dosing as adults. Rifapentine is not FDA-approved for treatment of tuberculosis disease in children less than 12 years of age		Cutaneous reactions, hematologic toxicity, GI symptoms, polyarthralgia, hepatotoxicity, pseudojaundice, flu-like symptoms, orange discoloration of body fluids
Rifabutin (RFB)	Adults: 5 mg/kg (300 mg) Children: unknown	Adults: Not recommended Children: unknown	Cutaneous reactions, GI reactions, flu-like symptoms, hepatotoxicity, severe immunologic reactions, orange discoloration of body fluids, drug interactions, uveitis

* Three times per week dosing is not used often and is reserved for certain circumstances. Please consult with a regional nurse consultant/TB expert.

HPMZ Four-Month Rifapentine-Moxifloxacin Treatment Regimen

Drug	Body Weight (kg)	Dose per day, mg	Adverse Reactions
Rifapentine (RPT)	Greater than or equal to 40 kg	1200 mg	Cutaneous reactions, hematologic toxicity, GI symptoms, polyarthralgia, hepatotoxicity, pseudojaundice, flu-like symptoms, orange discoloration of body fluids
Moxifloxacin (MOX)	Greater than or equal to 40 kg	400 mg	Nausea and diarrhea, headache and dizziness, rare tendon rupture, arthralgias, rare hepatotoxicity, QTc prolongation, hypo/hyperglycemia
Isoniazid (INH)	Greater than or equal to 40 kg	300 mg	Hepatic enzyme elevation, hepatitis, rash, peripheral neuropathy, mild central nervous system effects, drug interactions
Pyrazinamide (PZA)	40 kg to less than 55 kg	1000 mg	GI intolerance, hepatitis, rash, joint aches, hyperuricemia, gout (rare), photosensitivity
	Greater than or equal to 55 kg – 75 kg	1500 mg	
	Greater than 75 kg	2000 mg	

Treatment and Management

- Individuals living with HIV
  - RIF should not be used in patients who are receiving most anti-HIV protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs). RFB should be used in most instances; RFB dosage may need to be adjusted for concurrent administration of some anti-HIV PIs and NNRTIs. RIF may be used with nucleoside reverse transcriptase inhibitors (NRTIs). Please consult with an expert.
- RIPE treatment regimen
  - Doses should not be divided
  - Use EMB with caution in children whose vision cannot be monitored
  - Discontinue EMB when susceptibility to INH and RIF is demonstrated with good clinical response
  - Discontinue PZA after the Initial Phase - 8 weeks (see treatment table for number of doses) - unless there is resistance to either INH or RIF or lack of clinical response
- Drug resistance
  - Mono-drug resistant disease may require treatment regimen changes. Seek expert consultation.
  - Multi-drug resistant disease (resistant to INH and RIF) requires individualized treatment regimens and prolonged treatment. Seek expert consultation.
- Sputum monitoring
  - For pulmonary TB patients, perform sputum monitoring at least monthly until 2 consecutive sputum cultures become negative.
  - IDOH recommends consultation with a TB expert for anyone who is still sputum culture-positive at the end of the initial phase.
- Ongoing evaluation
  - Evaluate monthly for clinical improvement, medication side effects, and number of doses completed
  - Treatment completion is determined by both the number of doses and weeks of treatment completed
  - See 'Evaluation and Testing Considerations' table for further information.
- **NEVER add a single drug to a failing regimen. Please consult with an expert.**

Evaluation and Testing Considerations for Drug-susceptible Pulmonary TB Treatment Regimens

Evaluation and Testing Considerations	Four-month Rifapentine-Moxifloxacin Regimen	Standard Six-month RIPE Regimen
Rapid molecular testing	At baseline, test at least one specimen using a rapid molecular test. It is advisable to test at least one specimen using a rapid molecular test for susceptibility to • isoniazid (INH), • rifampin (RIF), as a proxy for rifapentine • pyrazinamide (PZA), and • fluoroquinolones	At baseline, test at least one specimen using a rapid molecular test. For patients with risk factors for drug-resistant disease, it is recommended to test at least one specimen using a rapid molecular test for susceptibility to • INH and • RIF
Acid-fast bacilli smear microscopy and culture	At baseline and at minimum monthly intervals until 2 consecutive specimens are negative on culture, test a respiratory specimen for acid-fast bacilli smear microscopy and culture	At baseline and at minimum monthly intervals until 2 consecutive specimens are negative on culture, test a respiratory specimen for acid-fast bacilli smear microscopy and culture
Phenotypic drug susceptibility testing	At baseline, obtain phenotypic (molecular and growth based) drug susceptibility at least for the following TB drugs • INH, • RIF, • PZA, and • fluoroquinolones (preferred fluoroquinolone is moxifloxacin)	At baseline, obtain phenotypic (molecular and growth based) drug susceptibility at least for the following TB drugs • INH, • RIF, • ethambutol, and • PZA
Additional tests	Recommended at baseline, obtain blood levels of • potassium, • calcium, and • magnesium	Not routinely recommended for all patients

Source: https://www.cdc.gov/tb/topic/treatment/tbdisease.htm (accessed Fall 2023)

TREATMENT REGIMENS FOR TB DISEASE CAUSED BY DRUG SUSCEPTIBLE ORGANISMS

	Initial (Intensive) Phase		Continuation Phase			
	Drugs	**Frequency and Duration**	**Drugs**	**Frequency and Duration**	**Total Doses**	**Comments**
PREFERRED	INH RIF PZA EMB *(See footnote A)*	7 days per week for 56 doses (8 weeks), or 5 days per week for 40 doses (8 weeks)[B]	INH RIF	7 days per week for 126 doses (18 weeks)[E], or 5 days per week for 90 doses (18 weeks)[B,E]	182 – 130	Commonly referred to as the **RIPE** regimen Pyridoxine (vitamin B6), 25-50 mg/day is given with INH to all persons at risk of neuropathy (e.g., pregnant individuals, breastfeeding infants, persons living with HIV, patients with diabetes, alcoholism, malnutrition, or chronic renal failure, or patients with advanced age). For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100 mg/day.
	RPT MOX INH PZA	7 days per week for 56 doses (8 weeks)[C]	RPT MOX INH	7 times per week for 63 doses (9 weeks)[D]	119	Recommended for people ages 12 and older with body weight at or above 40 kg, with pulmonary TB caused by organisms that are not known or suspected to be drug-resistant, and who have no contraindications to this regimen. The 4-month rifapentine-moxifloxacin TB treatment regimen is as effective as (noninferior to) the standard daily 6-month regimen in curing drug-susceptible TB disease. At least 5 of 7 weekly doses should be administered under direct observation. Pyridoxine (vitamin B6), 25-50 mg/day, should be given with isoniazid to all patients. Only for this regimen, drugs are administered with food once a day, every day of the week.
ALTERNATE	INH RIF PZA EMB *(See footnote A)*	7 days per week for 56 doses (8 weeks), or 5 days per week for 40 doses (8 weeks)[B]	INH RIF	3 times weekly for 54 doses (18 weeks)[E]	110 - 94	Preferred alternative regimen in situations (to RIPE in row 1) in which more frequent DOT during continuation phase is not possible. Pyridoxine (vitamin B6), 25-50 mg/day is given with INH to all persons at risk of neuropathy (e.g., pregnant individuals, breastfeeding infants, persons living with HIV, patients with diabetes, alcoholism, malnutrition, or chronic renal failure, or patients with advanced age). For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100 mg/day.

Abbreviations: INH – isoniazid, RIF – rifampin, PZA – pyrazinamide, EMB – ethambutol, RPT – rifapentine, MOX – moxifloxacin

[A] Other combinations may be appropriate in certain circumstances. Additional details: https://academic.oup.com/cid/article/63/7/e147/2196792

[B] Drugs may be given 5 days per week and the necessary number of doses adjusted accordingly. Although there are no studies that compare 5 with 7 daily doses, extensive experience indicates this would be an effective practice.

[C] Must be administered completely within 70 days from treatment initiation. If this target is not met, the patient should be considered to have interrupted therapy and should be managed as described in TB treatment guidelines: https://academic.oup.com/cid/article/63/7/853/2197067.

[D] Must be administered within 84 days from intensive phase completion. If this target is not met, the patient should be considered to have interrupted therapy and should be managed as described in https://academic.oup.com/cid/article/63/7/853/2197067.

[E] Based on expert opinion, patients with cavitation on the initial chest radiograph and positive cultures at completion of two months of therapy should receive a seven-month (31 week) continuation phase.

Note: Directly observed therapy (DOT) is the international standard of care and the medical standard of care in Indiana. DOT means that a healthcare worker watches the TB patient swallow each dose of the prescribed drugs. The healthcare worker should ask the patient how he or she is feeling, check the medications before they are taken, ask the patient if he or she is experiencing any side effects, and answer any questions the patient may have. Where local policies and circumstances allow for, electronic directly observed therapy (eDOT) in combination with in-person visits has been shown to be an acceptable alternative to traditional DOT. Consider consulting with a regional nurse consultant or TB expert as needed.