STANDARD TREATMENT REGIMENS FOR TB DISEASE CAUSED BY DRUG *SUSCEPTIBLE* ORGANISMS

Initial (Intensive) Phase			Continuation Phase				Regimen Effectiveness
Regimen	Drug[A]	Interval and Dose[B] (Minimum Duration)	Drugs	Interval and Dose[B, C] (Minimum Duration)	Range of Total Doses	Comments[C, D]	
1	INH RIF PZA EMB	7 days/week for 56 doses (8 weeks), or 5 days/week for 40 doses (8 weeks)	INH RIF	7 days/week for 126 doses (18 weeks), or 5 days/week for 90 doses (18 weeks)	182 – 130	This is the preferred regimen for patients with newly diagnosed pulmonary tuberculosis.	Greater
2	INH RIF PZA EMB	7 days/week for 56 doses (8 weeks), or 5 days/week for 40 doses (8 weeks)	INH RIF	3 times weekly for 54 doses (18 weeks)	110 - 94	Preferred alternative regimen in situations in which more frequent DOT during continuation phase is difficult to achieve	
3	INH RIF PZA EMB	3 times weekly for 24 doses (8 weeks)	INH RIF	3 times weekly for 54 doses (18 weeks)	78	Use regimen with caution in patients with HIV and/or cavitary disease. Missed doses can lead to treatment failure, relapse, and acquired drug resistance.	
4	INH RIF PZA EMB	7 days/week for 14 doses then twice weekly for 12 doses	INH RIF	Twice weekly for 36 doses (18 weeks)	62	The twice weekly regimen should be used with extreme caution and only in consultation with an expert. If doses are missed, then therapy is equivalent to once weekly, which is inferior. Do not use twice weekly regimens in HIV-infected patients or patients with smear positive and/or cavitary disease.	Lesser

Abbreviations: INH – isoniazid, RIF – rifampin, PZA – pyrazinamide, EMB – ethambutol, DOT – directly observed therapy, HIV – human immunodeficiency virus.

[A] Other combinations may be appropriate in certain circumstances.

[B] When DOT is used, 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. DOT should be used when drugs are administered <7 days per week.

[C] Based on expert opinion, patients with cavitation on initial chest radiograph and positive cultures at completion of 2 months of therapy should receive a 7-month (31 week) continuation phase.

[D] Pyridoxine (vitamin B6), 25-50 mg/day is given with INH to all persons at risk of neuropathy (e.g., pregnant women, breastfeeding infants, persons 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.

SUGGESTED PZA & EMB DOSES FOR ADULTS WEIGHING 40-90 Kg[a]

PZA	Weight (Kg)[b,c]			EMB	Weight (Kg)[b,c]		
	40-55	56-75	76-90		40-55	56-75	76-90
Daily	1000 mg	1500 mg	2000 mg	Daily	800 mg	1200 mg	1600 mg**
(mg/kg)	18.2-25.0	20.0-26.8	22.2-26.3	(mg/kg)	14.5-20.0	16.0-21.4	17.8-21.1
Thrice Weekly	1500 mg	2500 mg	3000 mg	Thrice Weekly	1200 mg	2000 mg	2400 mg**
(mg/kg)	27.3-37.5	33.3-44.6	33.3-39.5	(mg/kg)	21.8-30.0	26.7-35.7	26.7-31.6

[a] With normal renal function.

[b] Based on estimated lean body weight. Optimal doses for obese patients are not established.

[c] Range numbers are the calculated mg/kg doses for patients at the highest and lowest weights in the weight band.

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Treatment and Management of Tuberculosis Disease

Anti-Tuberculosis Drugs and Dosages for Adults[A] and Children[C]

Drug	Daily* (max)	3X Weekly (max)	Adverse Reactions
INH	A: 5 mg/kg (300 mg) C: 10-15 mg/kg (300 mg)	A: 15 mg/kg (900 mg) C: not established	Hepatic enzyme elevation, hepatitis,rash, peripheral neuropathy, mild CNS effects, drug interations
RIF	A: 10 mg/kg (600 mg) C: 10-20 mg/kg (600 mg)	A: 10 mg/kg (600 mg) C: not established	GI intolerance, drug interactions, hepatitis, bleeding problems, flu-like symptoms, orange discoloration of body fluids
RPT	A: 10 mg/kg (600 mg) C: Active Tuberculosis: for children ≥ 12 years of age, same dosing as adults. Rifapentine is not FDA- approved for treatment of active tuberculosis in children <12 years of age.		Hematologic toxicity, GI symptoms, polyarthralgia, hepatotoxicity, pseudojaundice, flu-like symptoms, orange discoloration of body fluids
RFB	A: 5 mg/kg (300 mg) C: unknown	A: Not recommended C: unknown	Cutaneous reactions, GI reactions, flu-like symptoms, hepatotoxicity, severe immunologic reactions, orange discoloration of body fluids, drug interactions, uveitis
PZA	A: see table on back C: 35 (30-40) mg/kg	A: see table on back C: not established	GI intolerance, Hepatitis, rash, joint aches, hyperuricemia, gout (rare)
EMB	A: see table on back C: 20 (15-25) mg/kg	A: see table on back C: not established	Optic neuritis

INH = isoniazid; RIF = rifampin; RPT = rifapentine; RFB = rifabutin; PZA = pyrazinamide; EMB = ethambutol; NRTIs = nucleoside reverse transcriptase inhibitors; NNRTIs = non-nucleoside reverse transcriptase inhibitors; PIs = protease inhibitors

*Daily therapy (or 5 times a week therapy in the continuation phase) has recently been shown to be more efficacious with less treatment failures than intermittent therapy (ATS/CDC/IDSA Clinical Practice Guidelines for Drug-Susceptible TB CID, 2016).

Suspect TB in patients with these symptoms:

- ✓ Prolonged productive cough that lasts 3 weeks or longer
- ✓ Night sweats
- ✓ Weight loss
- ✓ Hemoptysis
- ✓ Fatigue
- ✓ Loss of appetite

Especially if the patient:

- ✓ was identified as a contact to an infectious TB patient
- ✓ was born in or traveled to a country where TB is common
- ✓ has other social or demographic risk factors for TB exposure (homeless, incarceration)
- ✓ is HIV-positive, immunosuppressed or has other medical risk factors that increase the likelihood of progression to active disease if infected (end stage renal disease, diabetes, etc.)
- ✓ has a history of substance abuse of any kind
- ✓ has a positive Interferon-gamma release assay (IGRA) or tuberculin skin test

Pre-treatment Screening procedures:

- ✓ Obtain a PA & lateral chest x-ray.
- ✓ Place and read a tuberculin skin test using the Mantoux (intradermal) technique or draw blood for an IGRA (e.g., TSPOT, Quantiferon Gold).
- ✓ 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, culture, drug susceptibility and genotype testing.
- ✓ Test visual acuity and red-green color discrimination for those who will be taking ethambutol.
- ✓ 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.
- ✓ A history of BCG vaccination **is not** a contraindication for tuberculin skin testing.

TREATMENT AND MANAGEMENT

- ✓ **Begin treatment with 4 drugs**: INH, RIF, PZA, and EMB. **Doses should not be divided**. Use EMB with caution in children whose vision cannot be monitored.
- ✓ Directly observed therapy (DOT) is the international standard of care and the **medical standard of care in Indiana** and should be used for all patients.
- ✓ For pulmonary TB patients, perform sputum monitoring at least monthly until 2 consecutive sputum cultures become negative.
- ✓ Discontinue EMB when susceptibility to INH and RIF is demonstrated.
- ✓ Discontinue PZA after the **Initial Phase** –8 weeks (see treatment table on back for number of doses) unless there is resistance to either INH or RIF.
- ✓ Mono-drug resistant disease may require regimen changes. Seek expert consultation.
- ✓ Multi-drug resistant disease (resistant to INH and RIF) requires individualized regimens and prolonged treatment. **Seek expert consultation.**
- ✓ Extend the **Continuation Phase** from 18 to 31 weeks (see treatment table on back for number of doses) for patients with cavities on the chest radiograph or who are still culture-positive at the end of the Initial Phase or who did not receive PZA for the initial 8 weeks.
- ✓ ISDH recommends consultation with a TB expert for anyone who is still sputum culture-positive at the end of the Initial Phase (8 wks).
- ✓ Evaluate monthly for clinical improvement, medication side effects and number of doses completed.
- ✓ Perform follow-up laboratory tests if necessary; see indications for liver function testing later in this guide.
- ✓ HIV-infected patients: RIF should not be used in patients who are receiving most anti-HIV PIs and 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 NRTIs. **Please consult with an expert**.
- ✓ Treatment completion is determined by both the number of doses and weeks of treatment completed.
- ✓ **Never add a single drug to a failing regimen**. **Please consult with an expert.**

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