TREATMENT INFORMATION

- Tuberculosis treatment should always be undertaken in consultation with a physician who is **well-versed and experienced** in its management.
- All patients should be initially started on a 4-drug regimen of Isoniazid **(INH)**, Rifampin **(RIF)**, Pyrazinamide **(PZA)**, and Ethambutol **(EMB)**. Following the initial 8-week phase of treatment, the continuation phase should consist of **INH** and **RIF** in pansensitive cases.
- Directly Observed Therapy (DOT) is the international standard of care for all patients with TB disease and is essential for management of cases of multidrug-resistant TB (MDR-TB).
- Patients with TB should have monthly monitoring of sputum for AFB smear and culture, until negative.
- For all patients, drug susceptibility testing should be done on the initial *M. tuberculosis* isolate. Susceptibility testing should be repeated for patients who are not responding to therapy or who have positive cultures after 3 months of therapy.
- Treatment regimens for pulmonary TB are also effective for treating extrapulmonary TB.
- All new and suspected cases of active TB should be reported to state and/or local health departments.
- A single drug should never be added to a failing treatment regimen. Treatment of suspected drug-resistant TB should always include 2-3 new drugs.
- Based on medication history and drug susceptibility results, treatment for MDR-TB (i.e., resistance to at least INH and RIF) must be daily, individualized, and prolonged. **It is vital to seek expert consultation**.
- Treatment of tuberculosis benefits both the community as a whole and the individual patient; thus, any public health program or private provider must not only prescribe an appropriate regimen, but **also ensure adherence until treatment completion**.

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Treatment of Tuberculosis: Standard Therapy for Active Disease in Adults and Adolescents 2009

Based on the Official Joint Statement of the American Thoracic Society, Centers for Disease Control and Prevention, & Infectious Diseases Society of America, published in the Morbidity & Mortality Weekly Report, June 20, 2003.
This card is not intended as a complete reference for treatment of TB.

ANTI-TB DRUGS: FIRST-LINE MEDICATIONS – STANDARD THERAPY FOR ACTIVE DISEASE IN ADULTS & ADOLESCENTS

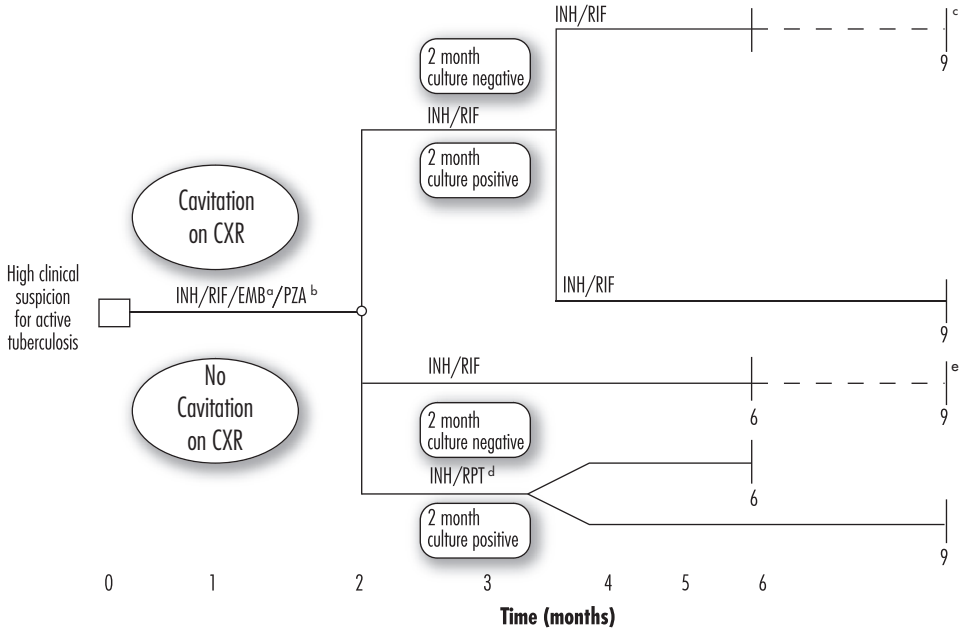
Treatment regimens that include four different first-line antituberculosis medications are recommended for the initial treatment of TB in adults. The initial regimen should include **INH**, **RIF**, **PZA**, and **EMB** unless there are contraindications to any of the drugs or if the patient is pregnant.[a] Rifampin should generally not be used in patients who are receiving HIV medications.

All antituberculosis medications should be given concurrently, as a single dose, in order to prevent development of resistant organisms and to enhance adherence, as well as achieve optimum drug serum levels. This card is not intended as a complete reference for treatment of tuberculosis.

DRUG	DOSAGES GIVEN IN MG/KG[b]; [MAXIMUM DOSE[c]]				Adverse Reactions	Monitoring	Comments
	Daily	Once Weekly[d]	2x Weekly[d]	3x Weekly[d]			
Isoniazid **INH:**[e] PO 	5 [300 mg]	15 [900 mg]	15 [900 mg]	15 [900 mg]	Hepatic enzyme elevation, hepatitis, rash, peripheral neuropathy, mild CNS effects, drug interactions	In patients with pre-existing liver disease or who develop abnormal liver function that does not require discontinuation of the drug; LFTs should be done monthly & when symptoms occur.	Hepatitis risk increases with age, alcohol use, & concurrent use of other hepatotoxic drugs. Supplementation with pyridoxine in patients with nutritional deficiency, medical conditions associated with peripheral neuropathy (i.e., diabetes, chronic renal failure/dialysis, HIV) and during pregnancy is recommended.
Rifampin **RIF:**[e] PO 	10 [600 mg]		10 [600 mg]	10 [600 mg]	GI intolerance, drug interactions, hepatitis, bleeding problems, flu-like symptoms, orange discoloration of bodily fluids	Drug interactions should be noted.[f]	Significant interactions with certain HIV medications, methadone, oral contraceptives, & other drugs.[f] Educate patients about normal discoloration of bodily fluids.
Rifapentine **RPT:** PO 		10-15 [600-900 mg] (continuation phase)			Hematologic toxicity, GI symptoms, polyarthralgia, hepatotoxicity, pseudojaundice, flu-like symptoms, orange discoloration of bodily fluids	Although drug interactions are less problematic than with RIF, they still require monitoring.	Used once weekly with INH, in the continuation phase only for HIV-seronegative patients with non-cavitary, drug-susceptible pulmonary TB who have negative sputum smears at 2 months.
Rifabutin* **RBT:** PO 	5 [300 mg]		5 [300 mg]	5 [300 mg]	Cutaneous reactions, GI reactions, flu-like symptoms, hepatotoxity, severe immunologic reactions, orange discoloration of bodily fluids, drug interactions due to induction of hepatic microsomal enzymes, uveitis	Although drug interactions are less problematic than with RIF, they still require monitoring.	Used as a substitute for RIF if patient demonstrates RIF intolerance or is taking drugs that have unacceptable interactions with RIF.
DRUG	**Patient's Weight**	**Daily**	**2x weekly**	**3x weekly**			
Pyrazinamide **PZA:**[e] PO 	40-55 kg	18.2-25.0 [1g]	36.4-50.0 [2 g]	27.3-37.5 [1.5 g]	Hepatitis, GI intolerance, rash, joint aches, hyperuricemia, gout (rare)	LFTs in patients with underling liver disease or in conjunction with RIF for treatment of LTBI; baseline uric acid.	Little information about safety of use in pregnancy. Reduce dose in patients with renal insufficiency.
	56-75 kg	20.0-26.8 [1.5 g]	40.0-53.6 [3 g]	33.3-44.6 [2.5 g]			
	76-90 kg	22.2-26.3 [2 g]	44.4-52.6 [4 g]	33.3-39.5 [3 g]			
Ethambutol **EMB:** PO 	40-55 kg	14.5-20.0 [.8 g]	36.4-50.0 [2 g]	21.8-30.0 [1.2 g]	Optic neuritis	Baseline visual acuity tests, color discrimination tests, and questioning each month.	Adjust dose or dosing internal when creatinine clearance is <30 ml/minute.
	56-75 kg	16.0-21.4 [1.2 g]	37.3-50.0 [2.8 g]	26.7-35.7 [2 g]			
	76-90 kg	17.8-21.1 [1.6 g]	44.4-52.6 [4 g]	26.7-31.6 [2.4 g]			

*[a]During pregnancy, initial regimen should include INH, RIF, EMB. A minimum of 9 months of therapy should be given. [b] Doses in mg/kg based on lean body weight. [c] Maximum dose regardless of weight. [d]All intermittent regimens must be directly observed. [e]Fixed-dose combinations of INH+RIF+PZA (Rifater®) and INH + RIF (Rifamate®) are preferred when DOT is not used. [f]See Morbidity & Mortality Weekly Report 52(RR-11), p. 47. *Not yet approved by the U.S. Food and Drug Administration for use in the treatment of tuberculosis.*

TREATMENT OF TUBERCULOSIS



[a]EMB may be discontinued when results of drug susceptibility testing indicate no drug resistance. [b]PZA may be discontinued after 2 months (56 doses). [c]With cavitation on initial CXR and 2-month culture being negative, therapy may be extended to 9 months at clinician's discretion. [d]RPT should not be used in HIV-infected patients with tuberculosis, in patients with extrapulmonary tuberculosis, or in patients with positive AFB smears at 2 months. [e]At clinician's discretion, therapy may be extended to 9 months if 2-month culture is positive.

DRUG REGIMENS FOR CULTURE-POSITIVE PULMONARY TUBERCULOSIS CAUSED BY DRUG-SUSCEPTIBLE ORGANISMS IN ADULTS

Consult the ATS/CDC/IDSA "Treatment of Tuberculosis" statement for more specific detail on the regimens listed below as well as alternative regimens not listed here.

MOST Preferred

	Initial Phase	Continuation Phase		
	Interval & Doses *(minimal duration)*		**Interval & Doses[a,b]** *(minimum duration)*	**Range of Total Doses** *(minimum duration)*
4 - Drug Combination		**2 - Drug Combination**		
INH RIF PZA EMB	7 days/wk for 56 doses (8 wks) or 5 days/wk for 40 doses (8 wks)	INH/RIF	7 days/wk for 126 doses (18 wks) or 5 days/wk for 90 doses (18 wks)	182-130 (26 wks)
		INH/RIF[c]	2x/wk for 36 doses (18 wks)	92-76 (26 wks)
		INH/RPT[d]	1x/wk for 18 doses (18 wks)	74-58 (26 wks)
INH RIF PZA EMB	7 days/wk for 14 doses (2 wks) then 2x/wk for 12 doses (6 wks) or 5 days/wk for 10 doses (2 wks) then 2x/wk for 12 doses (6 wks)	INH/RIF[c]	2x/wk for 36 doses (18 wks)	62-58 (26 wks)
		INH/RPT[d]	1x/wk for 18 doses (18 wks)	44-40 (26 wks)
INH RIF PZA EMB	3x/wk for 24 doses (8 wks)	INH/RIF	3x /wk for 54 doses (18 wks)	78 (26 wks)

[a]When DOT is used, drugs may be given 5 days/week & the necessary number of doses adjusted accordingly.
[b]Patients with cavitation on initial CXR & positive cultures at completion of 2 months of therapy should recieve a 7-month (31 weeks; either 217 doses [daily] or 62 doses [2x/week]) continuation phase.
[c]Not recommended for HIV-infected patients with CD4+ cell counts <100 cells/µl.
[d]Should only be used in HIV-negative patients who have negative sputum smears upon completion of 2 months of therapy & who do not have cavitation on initial chest radiograph. During this regimen, if 2-month specimen is culture positive, treatment should be extended an extra 3 months.

ANTI-TB DRUGS: SECOND-LINE MEDICATIONS: Since toxicities are greater when using second-line drugs, the following medications should **only** be used for patients with drug resistance or drug intolerance **in consultation with a physician experienced in the management of drug-resistant TB**. **Never add a single drug to a failing regimen**.

All patients with drug-resistant TB should be placed on directly observed therapy (DOT). Second-line drugs are not intended for intermittent use and should be given on a daily basis. Exercise extreme caution when using these drugs during pregnancy due to known and unknown risk to the fetus. The following drugs are listed alphabetically.

DRUG	Daily Dose [Max]	Adverse Reactions	Monitoring	Comments
Amikacin/kanamycin (AM/KM):* IM/IV	15 mg/kg [1 g][b]	Renal toxicity, vestibular dysfunction, hearing loss, electrolyte abnormalities, dizziness	Baseline and monthly auditory and renal function.	Avoid or reduce dose in adults over age 59 (10 mg/kg with a maximum dose of 750 mg). Should not be used concurrently with other aminoglycosides or Capreomycin.
Capreomycin (CM): IM/IV	15 mg/kg [1 g][b]	Auditory, vestibular, and renal toxicity, electrolyte abnormalities	Baseline and monthly auditory and renal function as well as serum K+ and Mg++ levels.	Avoid or reduce dose in adults over age 59 (10 mg/kg daily with maximum dose of 750 mg). Decrease dose with renal insufficiency. Should not be used with aminoglycosides.
Cycloserine (CS): PO	10-15 mg/kg [1 g]; 500-750 mg divided BID	CNS effects, peripheral neuritis, psychosis, seizures, depression, headaches, rash, drug interactions	Neuropsychiatric status assessed monthly.	Use cautiously in patients with renal insufficiency. Pyridoxine may decrease CNS effects. Avoid sunlight. Consider dosing at mealtimes. Although recommended, it is unusual for patients to tolerate this dosage. Drug serum concentration measurements are useful in determining the optimal dose.
Ethionamide (ETA): PO	15-20 mg/kg [1 g]; usually 500-750 mg QD or divided BID	GI intolerance, hepatotoxicity, neurotoxicity, endocrine effects, metallic taste, hypersensitivity	Baseline LFTs recommended in all patients. For patients with pre-existing liver disease or who develop abnormal liver function that does not require discontinuation of the drug, LFTs should be measured monthly & when symptoms occur.	Reduce dosage in patients with creatinine clearance of <30ml/min; start with low dosage and increase as tolerated. To reduce GI upset, give in divided dose. May cause hypothyroid condition, especially if used with PAS.
Levofloxacin (LEV):* PO/IV	500-750 mg	GI intolerance, headache, dizziness, rash, vaginitis, drug interactions, hypersensitivity		Cross resistance with Ciprofloxacin and Ofloxacin.[a] Should not be administered within 2 hours of taking antacid/medications containing divalent cations.
Moxifloxacin (MOX):* PO/IV	400 mg	GI intolerance, headache, dizziness, rash, vaginitis, drug interactions, hypersensitivity		Cross resistance with Ciprofloxacin and Ofloxacin.[a] Should not be administered within 2 hours of taking antacid/medications containing divalent cations.
p-Aminosalicylic acid (PAS): PO	8-12g in 2-3 doses	GI intolerance, hypersensitivity, hepatotoxicity, malabsorption syndrome, coagulopathy	Baseline hepatic enzymes and thyroid function.	May cause hypothyroid condition if used with ETA. Monitor cardiac patients for sodium load. Doubling of prothrombin time lessened with use of SM.
Streptomycin (SM): IM	15 mg/kg [1 g][b]	Ototoxicity (hearing loss or vestibular dysfunction), neurotoxicity, renal toxicity	Baseline hearing & serum creatinine measurement. Monthly renal function assessment and questioning regarding auditory or vestibular symptoms.	Avoid or reduce dose in adults over age 59 (10mg/kg daily with a maximum dose of 750 mg). Decrease dose with renal insufficiency.

*[a]Ciprofloxacin, Clarithromycin, Clofazimine, & Ofloxacin are not considered 2nd-line drugs, but can be used as alternatives to the listed options in cases of drug resistance/intolerance. [b] Usual dose is 750-1000 mg IV/IM; given as a single dose 5-7 days/week & reduced to 2-3 days/week after the first 2-4 months or after culture conversion, depending on efficacy of drug regimen. *Not yet approved by the U.S. Food and Drug Administration for use in the treatment of tuberculosis.*