Treatment of Drug-Susceptible Culture Confirmed Tuberculosis for Adults

First-Line TB Treatment Regimens

Regimen	Intensive Phase: Drug[a]	Intensive Phase: Interval and Dose[b] (Minimum Duration)	Continuation Phase: Drugs	Continuation Phase: Interval/Dose[b,c] (Minimum Duration)	Range of Total Doses	Comments[c,d]
1	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	7 d/wk for 126 doses (18 wk), or 5 d/wk for 90 doses (18 wk)	182-130	This is the preferred regimen for patients with newly diagnosed pulmonary tuberculosis.
2	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	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 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	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.

Regimen Effectiveness: Greater ↑ Lesser

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 (eg, pregnant women; breastfeeding infants; persons with HIV; patients with diabetes, alcoholism, malnutrition, or chronic renal failure; or patients with advanced age). Some patients with peripheral neuropathy may require a dose increase of pyridoxine to 100 mg daily.

DOT-Directly Observed Therapy **EMB**-Ethambutol **GI**-Gastrointestinal **INH**-Isoniazid **PZA**-Pyrazinamide **RIF**-Rifampin

Dosing Recommendations and Frequency

Drug	Preparation	Daily	Special Circumstances	Renal Dose Adjustment	Hepatic Dose Adjustment
Ethambutol[1]	100 mg tablets 100 mg tablets, coated 400 mg tablets, scored 400 mg tablets, coated and scored	**Standard dose:** 15-20 mg/kg daily	Pregnancy/breastfeeding: Safe in pregnancy; can be used while breastfeeding Renal disease: Use with caution; increased risk of toxicity with renal failure Hepatic disease: Safe in liver disease	**Est crcl < 30 ml/min:** 20-25 mg/kg 3x/weekly (not daily) (maximum 2400 mg 3x/weekly)	No dose adjustment
Isoniazid	50 mg, 100 mg, or 300 mg tablets scored or unscored 50 mg/5 ml oral suspension in sorbitol 100 mg/ml for IV or IM injection	**Standard dose:** 5 mg/kg daily (max 300 mg) and Vitamin B6 25-50 mg daily **Intermittent dose:** 15 mg/kg (max 900 mg) **High dose therapy:** 13-18 mg/kg daily	Pregnancy/breastfeeding: Safe during pregnancy; safe during breastfeeding Renal disease: Safe in renal disease; Vitamin B6 should be used	No dose adjustment	**Acute liver disease:** Avoid use **Stable hepatic disease:** Avoid if possible Close monitoring and periodic liver function testing
Pyrazinamide[2]	500 mg tablet, scored	**Standard dose:** 25-35 mg/kg daily	Pregnancy/breastfeeding: Risk/benefit should be discussed with pregnant women but should be used in drug-resistant TB when the isolate is susceptible to pyrazinamide; can be used while breastfeeding Renal disease: Cleared by the kidneys; dose 3 times a week and after dialysis Hepatic disease: Use with caution; pyrazinamide is associated with hepatotoxicity in about 1% of patients; can be severe and worsen off treatment	**Est crcl <30 ml/min:** 25-35 mg/kg (not daily) (maximum 3000 mg 3x/weekly)	**Moderate impairment:** Consider use with close monitoring, TDM, and periodic liver function testing
Rifabutin	150 mg capsule	**Standard dose:** 300 mg daily	Pregnancy/breastfeeding: Insufficient data in pregnancy; unknown effects from breastfeeding Renal disease: Use without dose adjustment in mild renal insufficiency; for creatinine clearance less than 30 ml/minute, the usual dose may be used, but monitor drug concentrations to avoid toxicity Hepatic disease: Use with caution Concomitant medications: Dosage adjustment may be required, particularly with anti-retroviral use	**Est crcl <30 ml/min:** Consider standard dose, but monitor drug concentrations to avoid toxicity Hemodialysis: Standard dosing	**Moderate impairment:** Consider use with close monitoring, TDM, and periodic liver function testing
Rifampin	150 mg or 300 mg capsules, powder may be suspended for immediate oral administration 600 mg/vial lyophilized powder for injection	**Standard dose:** 10 mg/kg daily 20 mg/kg or greater with TB Meningitis	Pregnancy/breastfeeding: Safe during pregnancy; can be used while breastfeeding Renal disease: Safe in renal disease Hepatic disease: Use with caution Concomitant medications: Dosage adjustment may be required for concurrent medications, including warfarin; concurrent treatment with most anti-retroviral drugs is not recommended, as most anti-retroviral drug concentrations are substantially reduced	No dose adjustment	**Moderate impairment:** Consider use with close monitoring, TDM, and periodic liver function testing

[1]Ethambutol Standard Dose Adjustment

	Weight		
	40-55 kg	56-75 kg	76-90 kg
Daily	800 mg	1200 mg	1600 mg
Twice-Weekly	2000 mg	2800 mg	4000 mg
Thrice-Weekly	1200 mg	2000 mg	2400 mg

[2]Pyrazinamide Standard Dose Adjustment

	Weight		
	40-55 kg	56-75 kg	76-90 kg
Daily	1000 mg	1500 mg	2000 mg
Twice-Weekly	2000 mg	3000 mg	4000 mg
Thrice-Weekly	1500 mg	2500 mg	3000 mg

Adverse Reactions and Monitoring

Drug	Adverse Reactions	Clinical Monitoring
Ethambutol	Ocular toxicity-optic neuritis (often manifested as decreased visual acuity or decreased red-green color discrimination) **Rare:** Peripheral neuropathy	Visual acuity (Snellen)/color-discrimination (Ishihara) assessment, baseline and monthly; ask about vision changes with each DOT dose
Isoniazid	Elevated liver enzymes (predominantly ALT and AST; may be asymptomatic or symptomatic), hepatitis, peripheral neurotoxicity, rash, arthralgia, drug induced lupus **Rare:** Hypersensitivity reactions	Monitor for clinical signs of hepatotoxicity (nausea, abdominal pain, jaundice, etc.) and neuropathy
Pyrazinamide	Polyarthralgia (non-gouty), asymptomatic hyperuricemia, hepatotoxicity, GI upset, self-limited transient morbilliform rash, photosensitive dermatitis **Rare:** Acute gout, usually in patients with pre-existing gout	Monitor for joint pain, GI adverse effects, and rash Monitor for clinical signs of hepatotoxicity (nausea, abdominal pain, jaundice, etc.)
Rifabutin	Rash/pruritis (generally self-limited), GI upset, hepatotoxicity, hematologic (leukopenia, neutropenia, thrombocytopenia), uveitis, arthralgias, fever **Note:** Rifabutin may produce an orange discoloration of body fluids (sweat, tears, urine, saliva) - this is NOT a toxicity and will resolve after treatment completion	Monitor for GI adverse effects, rash, and evidence of uveitis (eye redness or pain) Monitor closely for drug-drug interactions
Rifampin	Rash/pruritis, GI upset/nausea, hepatotoxicity (cholestatic picture) **Note:** Rifampin may produce an orange discoloration of body fluids (sweat, tears, urine, saliva) - this is NOT a toxicity and will resolve after treatment completion	Monitor for GI adverse effects and rash Monitor closely for drug-drug interactions

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This publication was supported by the Grant or Cooperative Agreement Number NU52PS910161 funded by the Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention or the Department of Health and Human Services.