

Table 2. Drug Regimens for Microbiologically Confirmed Pulmonary Tuberculosis Caused by Drug-Susceptible Organisms

Regimen	Drug ^a	Intensive Phase	Continuation Phase		Range of Total Doses	Comments ^{c,d}	Regimen Effectiveness
		Interval and Dose ^b (Minimum Duration)	Drugs	Interval and Dose ^{b,c} (Minimum Duration)			
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.	 Greater Lesser
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.	
4	INH RIF PZA EMB	7 d/wk for 14 doses then twice weekly for 12 doses ^e	INH RIF	Twice weekly for 36 doses (18 wk)	62	Do not use twice-weekly regimens in HIV-infected patients or patients with smear-positive and/or cavitary disease. If doses are missed, then therapy is equivalent to once weekly, which is inferior.	

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

^a Other combinations may be appropriate in certain circumstances; additional details are provided in the section “Recommended Treatment Regimens.”

^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). For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100 mg/day.

^e See [426]. Alternatively, some US tuberculosis control programs have administered intensive-phase regimens 5 days per week for 15 doses (3 weeks), then twice weekly for 12 doses.

rapport with the patient and for addressing treatment complications expeditiously, DOT remains the standard of practice in the majority of tuberculosis programs in the United States [33–35] and Europe [15] (Table 5). To be consistent with the principles of patient-centered care noted previously, decisions regarding the use of DOT must be made in concert with the patient [14–16]. For example, DOT can be provided in the office, clinic, or in the “field” (patient’s home, place of employment, school, or any other site that is mutually agreeable) by appropriately trained personnel [32].

PICO Question 2: Does self-administered therapy (SAT) have similar outcomes compared to directly observed therapy (DOT) in patients with various forms of tuberculosis?

Recommendation 2: We suggest using DOT rather than SAT for routine treatment of patients with all forms of tuberculosis (*conditional recommendation; low certainty in the evidence*).

RECOMMENDED TREATMENT REGIMENS

The preferred regimen for treating adults with tuberculosis caused by organisms that are not known or suspected to be drug resistant is a regimen consisting of an intensive phase of 2 months of isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB) followed by a continuation phase of 4 months of INH and RIF (see Tables 2, 3, 10, 11,

and Supplementary Appendix C) [3, 36, 37]. The intensive phase of treatment consists of 4 drugs (INH, RIF, PZA, EMB) because of the current proportion of new tuberculosis cases worldwide caused by organisms that are resistant to INH [38–41]; however, if therapy is being initiated after drug susceptibility test results are known and the patient’s isolate is susceptible to both INH and RIF, EMB is not necessary, and the intensive phase can consist of INH, RIF, and PZA only. EMB can be discontinued as soon as the results of drug susceptibility studies demonstrate that the isolate is susceptible to INH and RIF. Pyridoxine (vitamin B6) is given with INH to all persons at risk of neuropathy (eg, pregnant women; breastfeeding infants; persons infected with human immunodeficiency virus [HIV]; patients with diabetes, alcoholism, malnutrition, or chronic renal failure; or those who are of advanced age) [42, 43].

With respect to administration schedule, the preferred frequency is once daily for both the intensive and continuation phases (see PICO Questions 3 and 4 and Supplementary Appendix B, Evidence Profiles 5–11). Although administration of antituberculosis drugs using DOT 5 days a week has been reported in a large number of studies, it has not been compared with 7-day administration in a clinical trial. Nonetheless, on the basis of substantial clinical experience, experts believe that 5-days-a-week drug administration by DOT is an acceptable alternative to 7-days-a-week administration, and either approach