

Table 3 continued.

Drug	Preparation	Population	Daily	Once-Weekly	Twice-Weekly	Thrice-Weekly
Moxifloxacin	Tablets (400 mg); aqueous solution (400 mg/250 mL) for IV injection	Adults	400 mg daily	There are inadequate data to support intermittent administration. ¹		
		Children	The optimal dose is not known. Some experts use 10 mg/kg daily dosing, though lack of formulations makes such titration challenging. Aiming for serum concentrations of 3–5 µL/mL 2 h postdose is proposed by experts as a reasonable target.			

Abbreviations: FDA, US Food and Drug Administration; HIV, human immunodeficiency virus; IM, intramuscular; INH, isoniazid; IV, intravenous.

^a Dosing based on actual weight is acceptable in patients who are not obese. For obese patients (>20% above ideal body weight [IBW]), dosing based on IBW may be preferred for initial doses. Some clinicians prefer a modified IBW ($IBW + [0.40 \times (\text{actual weight} - IBW)]$) as is done for initial aminoglycoside doses. Because tuberculosis drug dosing for obese patients has not been established, therapeutic drug monitoring may be considered for such patients.

^b For purposes of this document, adult dosing begins at age 15 years or at a weight of >40 kg in younger children. The optimal doses for thrice-weekly therapy in children and adolescents have not been established. Some experts use in adolescents the same doses as recommended for adults, and for younger children the same doses as recommended for twice-weekly therapy.

^c Higher doses of rifampin, currently as high as 35 mg/kg, are being studied in clinical trials.

^d Rifabutin dose may need to be adjusted when there is concomitant use of protease inhibitors or nonnucleoside reverse transcriptase inhibitors.

^e TBTC Study 22 used rifapentine (RPT) dosage of 10 mg/kg in the continuation phase of treatment for active disease [9]. However, RIFAQUIN and PREVENT TB safely used higher dosages of RPT, administered once weekly [164, 210]. Daily doses of 1200 mg RPT are being studied in clinical trials for active tuberculosis disease.

^f As an approach to avoiding ethambutol (EMB) ocular toxicity, some clinicians use a 3-drug regimen (INH, rifampin, and pyrazinamide) in the initial 2 months of treatment for children who are HIV-uninfected, have no prior tuberculosis treatment history, are living in an area of low prevalence of drug-resistant tuberculosis, and have no exposure to an individual from an area of high prevalence of drug-resistant tuberculosis. However, because the prevalence of and risk for drug-resistant tuberculosis can be difficult to ascertain, the American Academy of Pediatrics and most experts include EMB as part of the intensive-phase regimen for children with tuberculosis.

^g Clinicians experienced with using cycloserine suggest starting with 250 mg once daily and gradually increasing as tolerated. Serum concentrations often are useful in determining the appropriate dose for a given patient. Few patients tolerate 500 mg twice daily.

^h Ethionamide can be given at bedtime or with a main meal in an attempt to reduce nausea. Clinicians experienced with using ethionamide suggest starting with 250 mg once daily and gradually increasing as tolerated. Serum concentrations may be useful in determining the appropriate dose for a given patient. Few patients tolerate 500 mg twice daily.

[†] Modified from adult intermittent dose of 25 mg/kg, and accounting for larger total body water content and faster clearance of injectable drugs in most children. Dosing can be guided by serum concentrations.

[‡] RIFAQUIN trial studied a 6-month regimen. Daily isoniazid was replaced by daily moxifloxacin 400 mg for the first 2 months, followed by once-weekly doses of moxifloxacin 400 mg and RPT 1200 mg for the remaining 4 months. Two hundred twelve patients were studied (each dose of RPT was preceded by a meal of 2 hard-boiled eggs and bread). This regimen was shown to be noninferior to a standard daily administered 6-month regimen [164].

may be considered as meeting the definition of “daily” dosing. There are alternative regimens that are variations of the preferred regimen, which may be acceptable in certain clinical and/or public health situations (see “Other Regimens” and “Treatment in Special Situations” in the full-text version of the guideline).

PICO Question 3: Does intermittent dosing in the intensive phase have similar outcomes compared to daily dosing in the intensive phase for treatment of drug-susceptible pulmonary tuberculosis?

Recommendation 3a: We recommend the use of daily rather than intermittent dosing in the intensive phase of therapy for drug-susceptible pulmonary tuberculosis (*strong recommendation; moderate certainty in the evidence*).

Recommendation 3b: Use of thrice-weekly therapy in the intensive phase (with or without an initial 2 weeks of daily therapy) may be considered in patients who are not HIV infected and are also at low risk of relapse (pulmonary tuberculosis caused by drug-susceptible organisms, that at the start of treatment is noncavitary and/or smear negative) (*conditional recommendation; low certainty in the evidence*).

Recommendation 3c: In situations where daily or thrice-weekly DOT therapy is difficult to achieve, use of twice-weekly therapy after an initial 2 weeks of daily therapy may be considered for patients who are not HIV-infected and are also at low risk of relapse (pulmonary tuberculosis caused by drug-susceptible organisms, that at the start of treatment is noncavitary and/or smear negative) (*conditional recommendation; very low certainty in the evidence*). Note: If doses are missed in a regimen using twice-weekly dosing, then therapy is equivalent to once weekly, which is inferior (see PICO Question 4).

Table 4. Possible Components of a Multifaceted, Patient-Centered Treatment Strategy

Enablers	Incentives
Interventions to assist the patient in completing therapy [130]	Interventions to motivate the patient, tailored to individual patient wishes and needs and, thus, meaningful to the patient [130]
Transportation vouchers [30]	Food stamps or snacks and meals [30]
Convenient clinic hours and locations [30]	Restaurant and grocery store coupons [30]
Clinic personnel who speak the languages of the populations served [428]	Assistance in finding or provision of housing [429]
Reminder systems and follow-up of missed appointments [28]	Clothing or other personal products [30]
Social service assistance (referrals for substance abuse treatment and counseling, housing, and other services) [429]	Books [428]
Outreach workers (bilingual/bicultural as needed; can provide many services related to maintaining patient adherence, including provision of directly observed therapy, follow-up on missed appointments, monthly monitoring, transportation, sputum collection, social service assistance, and educational reinforcement) [428]	Stipends [30]
Integration of care for tuberculosis with care for other conditions [428]	Patient contract [30]