Table 12. Dosing Recommendations for Adult Patients With Reduced Renal Function[a]

Drug	Change in Frequency?	Recommended Dose and Frequency for Patients With Creatinine Clearance <30 mL/min, or Patients Receiving Hemodialysis
Isoniazid	No	300 mg once daily, or 900 mg 3 times/wk
Rifampin	No	600 mg once daily, or 600 mg 3 times/wk
Pyrazinamide	Yes	25–35 mg/kg/dose 3 times/wk (not daily)
Ethambutol	Yes	20–25 mg/kg/dose 3 times/wk (not daily)
Levofloxacin	Yes	750–1000 mg/dose 3 times/wk (not daily)
Moxifloxacin	No	400 mg once daily
Cycloserine	Yes	250 mg once daily, or 500 mg/dose 3 times/wk[b]
Ethionamide	No	250–500 mg/dose daily
Para-amino salicylic acid	No	4 g/dose twice daily
Streptomycin	Yes	15 mg/kg/dose 2-3 times/wk (not daily)
Capreomycin	Yes	15 mg/kg/dose 2-3 times/wk (not daily)
Kanamycin	Yes	15 mg/kg/dose 2-3 times/wk (not daily)
Amikacin	Yes	15 mg/kg/dose 2-3 times/wk (not daily)

- Standard doses are given unless there is intolerance.
- The medications should be given after hemodialysis on the day of hemodialysis.
- Monitoring of serum drug concentrations should be considered to ensure adequate drug absorption, without excessive accumulation, and to assist in avoiding toxicity.
- Data currently are not available for patients receiving peritoneal dialysis. Until data become available, begin with doses recommended for patients receiving hemodialysis and verify adequacy of dosing using serum concentration monitoring.
- In patients with 30–50 mL/min creatinine clearance, standard doses are used by experts, but measurement of serum concentrations 2 and 6 hours after timed administration can be used to assist with optimizing drug dosages.

[a] Including adult patients receiving hemodialysis.

[b] The appropriateness of 250-mg daily doses has not been established. There should be careful monitoring for evidence of neurotoxicity.

conditions that could affect drug absorption, such as diabetes mellitus with gastroparesis. For patients receiving peritoneal dialysis, there is currently a paucity of pharmacokinetic and dosing data, and the dosages in Table 12 may not apply to patients receiving peritoneal dialysis. Such patients may require close monitoring for toxicity, and measurements of the serum concentrations of antituberculosis drugs before and after peritoneal dialysis should be considered.

Hepatic Disease

Tuberculosis treatment in patients with preexisting advanced liver disease poses significant challenges. The likelihood of drug-induced hepatitis is increased with prior advanced liver disease [364], liver transplant [365], or hepatitis C infection [366, 367]. Abnormal baseline aminotransferases alone are an independent risk factor for DILI [364, 368]. Experts recommend that patients with a history of injection drug use, birth in Asia or Africa (or other hepatitis virus endemic regions), or HIV infection have hepatitis B and C virus screening at baseline (Table 7). For patients with marginal hepatic reserve, superimposed DILI [56] may be severe, even life-threatening [369]. Fluctuations of serum aminotransferases and total bilirubin from preexisting liver disease can confound monitoring for DILI. Hepatic tuberculosis may also cause elevated aminotransferases, which improve with effective tuberculosis treatment.

Regimens with fewer potentially hepatotoxic agents are selected in patients with advanced liver disease or whose serum ALT is >3 times the upper limit of normal at baseline (and not thought to be caused by tuberculosis). The crucial efficacy of INH and particularly RIF warrant their use and retention, if at all possible, even in the face of preexisting liver disease. Expert consultation is advisable. Adjustments during treatment may be necessary. Drug susceptibility testing to fluoroquinolones and injectables is indicated if use of these drugs is being considered.

Alternative regimens for use in patients with hepatic disease include:

- Treatment without PZA: PZA has often been implicated in DILI. A potential regimen could be INH, RIF, and EMB for 2 months, followed by 7 months of INH and RIF [370, 371].
- Treatment without INH and PZA: For advanced liver disease patients, RIF and EMB with a fluoroquinolone, injectable, or cycloserine for 12–18 months, depending on the extent of the disease and response could be considered [372].
- Treatment without INH: Based on outcomes of studies on INH-resistant tuberculosis, a regimen of RIF, PZA, and EMB with or without a fluoroquinolone could be considered for a total duration of at least 6 months [373]. Although this regimen has 2 potentially hepatotoxic medications, it has the advantage of retaining a treatment duration of 6 months.
- Regimens with little or no potential hepatotoxicity: For patients with severe, unstable liver disease, EMB combined with a fluoroquinolone, cycloserine, and second-line injectable for 18–24 months (similar to an multidrug-resistant tuberculosis regimen) can be considered [374]. Some experts avoid aminoglycosides in patients with severe, unstable liver disease due to concerns about renal insufficiency or bleeding from the site of injected medication due to thrombocytopenia and/or coagulopathy.