

drug regimen. More recent evidence also suggests that completion rates of a self-administered 3-month regimen of weekly isoniazid and rifapentine are noninferior to those seen with DOT in the United States. It is expected that a 1-month daily regimen in combination with rifapentine will be added to new WHO guidelines.

For treatment of TB disease, isoniazid is used in combination with other agents to ensure killing of both actively dividing *M. tuberculosis* and slowly growing “persister” mycobacteria. Unless the organism is resistant, the standard regimen includes isoniazid, rifampin, ethambutol, and pyrazinamide ([Table 181-2](#)). Isoniazid is often given together with 25–50 mg of pyridoxine daily to prevent drug-related peripheral neuropathy.

MECHANISM OF ACTION Isoniazid is a prodrug activated by the mycobacterial KatG catalase-peroxidase; isoniazid is coupled with reduced nicotinamide adenine dinucleotide (NADH). The resulting isonicotinic acyl–NADH complex blocks the mycobacterial ketoenoylreductase known as InhA through binding to its substrate and inhibiting fatty acid synthase and ultimately mycolic acid synthesis. Mycolic acids are essential components of the mycobacterial cell wall. KatG activation of isoniazid also results in the release of free radicals that have antimycobacterial activity, including nitric oxide.

The minimal inhibitory concentrations (MICs) of isoniazid for wild-type (untreated) susceptible strains are <0.1 µg/mL for *M. tuberculosis* and 0.5–2 µg/mL for *M. kansasii*.

PHARMACOLOGY Isoniazid is the hydrazide of isonicotinic acid, a small, water-soluble molecule. The usual adult oral daily dose of 300 mg results in peak serum levels of 3–5 µg/mL within 30 min to 2 h after ingestion—well in excess of the MICs for most susceptible strains of *M. tuberculosis*. Both oral and IM preparations of isoniazid reach effective levels in the body, although antacids and high-carbohydrate meals may interfere with oral absorption. Isoniazid diffuses well throughout the body, reaching therapeutic concentrations in body cavities and fluids, with concentrations in cerebrospinal fluid (CSF) comparable to those in serum.