

Bedaquiline added to a background regimen improved the 2-month sputum culture–conversion rate in multicenter, randomized placebo-controlled trials, and these results led to approval by the U.S. Food and Drug Administration (FDA). However, the death rate in one trial was higher in the bedaquiline arm than in the control arm (11.4% vs 2.5%); the result was a “black box” warning from the FDA, which also included QT prolongation. Subsequent studies have not found an association with significant mortality. The CDC has made a provisional recommendation for the use of bedaquiline for 24 weeks in adults with laboratory-confirmed pulmonary MDR-TB when no other effective treatment regimen can be provided. Bedaquiline is an integral part of all shorter course, oral MDR treatment regimens endorsed by the WHO.

OXAZOLIDINONES Linezolid is an oxazolidinone used primarily for the treatment of drug-resistant gram-positive bacterial infections. However, this drug is active in vitro against *M. tuberculosis* and NTM. Several case series have suggested that linezolid may help clear mycobacteria relatively rapidly when included in a regimen for the treatment of complex cases of drug-resistant TB. Linezolid’s mechanism of action is disruption of protein synthesis by binding to the 50S bacterial ribosome. Linezolid has nearly 100% oral bioavailability, with good penetration into tissues and fluids, including CSF. Clinical resistance to linezolid has been reported and is typically associated with mutations in the 23S rRNA and in two ribosomal proteins, L3 (*rpIC*) and L4 (*rpID*). Adverse effects may include optic and peripheral neuropathy, pancytopenia, and lactic acidosis and are usually associated with higher doses. Linezolid is a weak monoamine oxidase inhibitor and can be associated with the serotonin syndrome when given concomitantly with serotonergic drugs (primarily antidepressants such as selective serotonin reuptake inhibitors). It has been shown that ~80% of patients with MDR-TB can be successfully treated with linezolid-containing, individualized anti-TB regimens based on drug sensitivity testing. Replacement of ethambutol with linezolid for 2–4 weeks during the intensive phase of treatment of drug-susceptible TB is currently being evaluated for possible faster sputum conversion and a shorter