

Characteristics of Second-line Drugs for MDR-TB^a

Drug	Bactericidal	MIC (ug/ml)	Serum Level	Dosing	Remarks	Side Effects
Rifabutin	Yes	0.25-0.5	0.3-0.9	300-450 mg daily	Extensive drug interactions: P-450 induction (less than rifampin) decreases levels of protease inhibitors, methadone, oral contraceptives, diabetic medications, fluconazole, and others: see PDR ^b Concentrates in macrophages.	Decreased white blood cell count, decreased platelet count, arthralgias, renal impairment, hyperpigmentation, uveitis, discoloration of body fluids, flushing erythema of the head and trunk, gastrointestinal upset, hepatitis, ageusia
Levofloxacin	Yes	0.5-1.0	8-12	500-1,000 mg daily (usually 750 mg)	L isomer - all active drug; Adjust dose with renal failure	Gastrointestinal upset, dizziness, hypersensitivity, photosensitivity, headaches, tendonitis, tendon rupture, insomnia, psychosis, agitation, depression, paranoia, seizures, thrush, hepatitis, peripheral neuropathy.
Moxifloxacin	Yes	0.25	4-6	400 mg daily	Good CNS penetration; No dose adjustment with renal failure; May increase liver enzymes	Ototoxicity - auditory/vestibular (irreversible), renal toxicity, pain at injection site.
Amikacin	Yes	0.5-1.0	25-35	Adult Initial dosing: 15mg - 1kg/day 5-7 days/wk After conversion: 20-25 mg/kg 2-3 days/wk	Vestibular screen, baseline, and monthly audiogram; Monitor creatinine; Adjust dose and/or interval for renal insufficiency.	Ototoxicity - auditory/vestibular, hypokalemia, hypocalcemia, hypomagnesemia, pain at injection site.
Capreomycin	Yes	1.25-2.5	~25	>59 years: 10 mg/kg (max 750 mg) 5 days per week or 2-3 times per week after initial period		Ototoxicity - auditory/vestibular (irreversible), renal toxicity, giddiness, perioral numbness, hypersensitivity, pain at injection site.
Streptomycin	Yes	0.25-2.0	25-35	Renal Failure: 12-15 mg/kg after dialysis 2-3 times weekly		
Cycloserine	No	NA ^c	20-35		Avoid in patients with seizures/psychotic disease or ETOH abuse; Check level before increasing dose >500 mg daily; Adjust dose with renal failure; Administer with pyridoxine 50-100 mg daily	Agitation, psychosis, depression, seizures, dizziness, headache, slurred speech, insomnia.
Ethionamide	Weak	0.3-1.2	1.5	250 mg 2 times daily or 250 mg a.m./500 mg p.m.	Increase dose gradually; Monitor liver function/thyroid function; Increases effect of cycloserine.	Peripheral neuropathy, abdominal pain, nausea, vomiting, hypothyroidism, salivation, metallic taste, hepatitis, giddiness, headache, hypersensitivity, alopecia, gyneocomastia, hypotension, impotence, mental disturbance, menstrual irregularity, hypoglycemia, photosensitivity.
Linezolid	Unkown	0.25-0.5	12-24	600 mg daily	Pyridoxine 50 mg daily	Peripheral neuropathy, optic neuritis (reversible), anemia, thrombocytopenia, neutropenia, headache, GI upset, rash, serotonin syndrome, lactic acidosis.
Clofazamine	Weak	0.12	0.5-2.0	100 mg daily	Skin problems; can be limited by sunscreen and lubricants	QTC prolongation Hyperpigmentation, GI complaints, acne flare, retinopathy, ichthyosis.
Bedaquiline	Yes	0.125	NA	400 mg daily for 14 days; then 200 mg 3 times/wk for 22 weeks (may give longer); Give with meal to increase bioavailability	No dose adjustment with renal or liver disease; EKG baseline and at least at 2, 12, and 24 weeks; Stop if QTc >500; Monitor potassium, calcium, and magnesium, TSH	QTC prolongation, decreased appetite, nausea, hepatitis, headaches, arthralgias.
Delamanid	Yes	0.003-0.024	NA	100 mg 2 times weekly for 24 weeks (longer is possible)	EKG baseline and at least 2,12, and 24 weeks; Stop if QTc >500; Monitor potassium, calcium, and magnesium	QTC prolongation, nausea, vomiting, dizziness, insomnia, upper abdominal pain.
Meropenem	Yes	<1.0	NA	1 g every 8-12 hours intravenously with clavulanate (given as amoxicillin-clavulanate 250 mg/125 mg every 8-12 hours)	Adjust dose with renal failure	Nausea, vomiting, gastrointestinal upset, rarely increased liver enzymes.
INH (High Dose)	Yes	<5.0	NA	15-20 mg/kg daily	Pyridoxine 50 mg daily, interacts with phenytoin; Useful only if MIC is <5.0 ug/ml	Optic neuritis, positive ANA ^d rash, fever, jaundice, hepatitis, peripheral neuritis, anemia, agranulocytosis, decreased platelets, vasculitis.

^aadult-type disease; ^bPDR, Physicians Desk Reference, 64th ed., 2010; ^cNA, not available; ^dANA, antinuclear antibody

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