

## CHARACTERISTICS OF SECOND-LINE DRUGS FOR MDR-TB<sup>a</sup>

Drug	Bactericidal	MIC (ug/ml)	Serum Level	Dosing	Remarks	Side Effects
<b>Rifabutin</b>	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 <sup>b</sup> : 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, taste alterations.
<b>Levofloxacin</b>	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.
<b>Moxifloxacin</b>	Yes	0.25	4-6	400 mg daily	Good CNS penetration; No dose adjustment with renal failure; May increase liver enzymes	
<b>Amikacin</b>	Yes	0.5-1.0	25-35			Ototoxicity - auditory/vestibular (irreversible), renal toxicity, pain at injection site.
<b>Capreomycin</b>	Yes	1.25-2.5	~25	Initial dosing: 15mg/kg daily 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 (irreversible), hypokalemia, hypocalcemia, hypomagnesemia, pain at injection site.
<b>Streptomycin</b>	Yes	0.25-2.0	25-35			Ototoxicity - auditory/vestibular (irreversible), renal toxicity, giddiness, perioral numbness, hypersensitivity, pain at injection site.
<b>Cycloserine</b>	No	NA <sup>c</sup>	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.	Agitation, psychosis, depression, seizures, dizziness, headache, slurred speech, insomnia.
<b>Ethionamide</b>	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.
<b>Linezolid</b>	Unkown	0.25-0.5	12-24	600 mg daily	Pyridoxine 100 mg daily	Peripheral neuropathy, optic neuritis (reversible), anemia, thrombocytopenia, neutropenia, headache, GI upset, rash, serotonin syndrome, lactic acidosis.
<b>Clofazamine</b>	Weak	0.12	0.5-2.0	100 mg daily	Skin problems; can be limited by sunscreen and lubricants	Hyperpigmentation, GI complaints, acne flare, retinopathy, ichthyosis, sunburn.
<b>Bedaquiline</b>	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 at 2, 12, and 24 weeks; Stop if QTc >500; Monitor potassium, calcium, and magnesium	QTc prolongation, decreased appetite, nausea, hepatitis, headaches, arthralgias.
<b>Delamanid</b>	Yes	0.003-0.024	NA	100 mg 2 times weekly for 24 weeks (longer is possible)	EKG baseline at 2,12, and 24 weeks; Stop if QTc >500; Monitor potassium, calcium, and magnesium	QTc prolongation, nausea, vomiting, dizziness, insomnia, upper abdominal pain.
<b>Meropenem</b>	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.
<b>PAS</b>	No	8.0	20-60 (6 h after dose)	4 g 2-3 times daily	Diarrhea improves with time; increase dose gradually over first 7 - 10 days, mix with acidic juice or applesauce; Avoid diphenhydramine	Gastrointestinal upset, diarrhea (self-limiting), hypothyroidism, hypokalemia, hepatitis, thrombocytopenia, increased acidosis in patients with renal failure.
<b>INH (High Dose)</b>	Yes	<5.0	NA	15-20 mg/kg daily	Pyridoxine 100 mg daily, interacts with phenytoin; Useful only if MIC is <5.0 ug/ml	Optic neuritis, positive ANA <sup>d</sup> rash, fever, jaundice, hepatitis, peripheral neuritis, anemia, agranulocytosis, decreased platelets, vasculitis.

<sup>a</sup>adult-type disease; <sup>b</sup>PDR, Physicians Desk Reference, 64th ed., 2010; <sup>c</sup>NA, not available; <sup>d</sup>ANA, antinuclear antibody

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