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CURRY INTERNATIONAL TUBERCULOSIS CENTER

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Medication Fact Sheets

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AMIKACIN (AK) [1 of 2]

Drug class	Aminoglycoside
Trade name	Amikacin/Amikin
Activity against TB	**Bactericidal.**
Cross-resistance	Kanamycin; variable frequency of cross-resistance with capreomycin has been reported
Dose	**Adults:** 15 mg/kg/day in a single daily dose, 5–7 days/ week Some experts suggest 15 mg/kg/dose, 2-3x/week can be used after culture conversion is documented and after initial period of daily administration (some experts use up to 25 mg/kg/dose for intermittent therapy). **> 59 years of age:** Many experienced clinicians prefer to use a lower starting dose of 10 mg/kg/dose (max 750mg) 5-7x/week or 2-3 x/week after initial period and consider follow-up measurement of drug concentration. **Children:** [Sentinel Project 2022, ATS/CDC/ERS/IDSA 2019] 15-20 mg/kg/day (max 1000 mg/day); 5-7 days/week **Renal failure:** 15 mg/kg 2-3x/week (not daily); dose after hemodialysis. **Obesity:** Dose should be adjusted due to the decreased distribution of extracellular fluids in adipose tissues. Dosing based on actual weight will give supratherapeutic concentrations. For dosing in obesity, use adjusted weight as follows: Ideal body weight + 40% of excess weight Ideal body weight (men): 50 kg plus 2.3 kg/inch over 5 ft ideal body weight (women): 45 kg plus 2.3 kg/inch over 5 ft Serum drug concentrations should be used to ensure appropriate drug exposure and clearance, see ***Pharmacokinetics*** below for timing and **Chapter 4, *Treatment***, section on ***Therapeutic Drug Monitoring***. Concentrations should be followed closely.
Route of administration	IV or IM (intraperitoneal and intrathecal have been reported). Some report that it is more painful than IM streptomycin. Not absorbed orally. Useful resource: Heartland National TB Center's *Administration of Amikacin Injection* tool. https://www.heartlandntbc.org/wp-content/uploads/2021/12/administration_of_amikacin_injection.pdf
Preparation	Colorless solution; 250 mg/mL (2-, 3-, or 4-mL vials) and 50 mg/mL (2-mL vial). For intravenous solution, mix with D5W or other solutions (in at least 100 mL of fluid for adults or 5 mg/mL for children).
Storage	Solution in original vial is stable at room temperature; diluted solution is stable at room temperature at least 3 weeks or in the refrigerator at least 60 days.
Pharmacokinetics	For intravenous administration, infuse over 30-60 minutes for adults; 1–2 hours for children; intramuscular absorption is complete within 4 hours and peak concentrations are achieved at 1–2 hours. Intramuscular absorption might be delayed if the same site is used consistently. Obtaining a drug concentration 2 and 6 hours post dose provides complete information for calculating C_{max}, C_{min}, and half-life. A trough concentration is generally not necessary if 2- and 6-hour concentrations are measured. Nomogram dosing and random sampling late in the dosing interval are discouraged. **Peak concentrations** for a 15 mg/kg dose are between 35 - 45 mcg/mL. **Peak concentrations** for a 25 mg/kg dose are between 65 - 80 mcg/mL. **Trough concentrations** are generally < 5 mcg/mL in patients with normal renal function. **Blood sampling times:** 2 and 6 hours post dose. **Half-life:** 2-3 hours with normal renal function.

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AMIKACIN (AK) [2 of 2]

Oral absorption	There is no significant oral absorption.
CSF penetration	Variable penetration; appears to penetrate inflamed meninges better.
Special circumstances	**Use in pregnancy/breastfeeding:** Generally avoided in pregnancy due to congenital deafness seen with streptomycin and kanamycin. Can be used while breastfeeding. Use in renal disease: Use with caution. Concentrations should be monitored for patients with impaired renal function. Interval adjustment is recommended for renal impairment or hemodialysis. See "Dose – Renal Failure" (previous page). The drug is variably cleared by hemodialysis. **Use in hepatic disease:** Drug concentrations not affected by hepatic disease (except a larger volume of distribution for patients with alcoholic cirrhosis and ascites). Presumed to be safe in severe liver disease; however, use with caution—some patients with severe liver disease may progress rapidly to hepato-renal syndrome. **Diuretic use:** Coadministration of loop diuretics and aminoglycoside antibiotics carries an increased risk of ototoxicity.
Adverse reactions	• Nephrotoxicity: Monitor BUN and serum creatinine. • Ototoxicity (hearing loss): Increased with advanced age and prolonged use. • Vestibular toxicity • Local pain with IM injections • Electrolyte abnormalities, including hypokalemia, hypocalcemia, and hypomagnesemia
Contraindications	**Pregnancy**—relative contraindication (congenital deafness seen with streptomycin and kanamycin use in pregnancy). **Hypersensitivity to aminoglycosides.** **Caution with renal, hepatic, vestibular, or auditory impairment.**
Monitoring	Monitor renal function by documenting creatinine at least monthly (more frequently if renal or hepatic impairment); document creatinine clearance if there is baseline renal impairment or any concerns; document baseline and monthly audiology exam; follow monthly electrolytes, magnesium, and calcium. Question patient regularly about vestibular complaints and perform serial vestibular exams. Document peak and trough concentrations at baseline if there is any question about renal function. Some experts monitor aminoglycoside concentrations routinely until one month after medication discontinuation, regardless of renal function. Monitor concentrations serially for patients with impaired renal function.
2022 wholesale cost 30-day supply, 60-kg person	$110 (outpatient public health pricing, 340B)
Patient instructions	**Call your doctor right away if you have:** • Changes in your hearing, or ringing or fullness in your ears • Dizziness, weakness, or unsteadiness • Trouble breathing • Swelling of feet or ankles • Decreased urination • Swelling, pain, or redness at your IV site • Muscle twitching or weakness

AMOXICILLIN/CLAVULANATE (AMX/CLV) [1 of 2]

Drug class	Penicillin/beta-lactam inhibitor [use **only** when added to a carbapenem]
Trade name	Augmentin or Augmentin ES-600 suspension
Activity against TB	Only used for clavulanate portion as adjunct with a carbapenem such as imipenem/cilastatin and meropenem for role as beta-lactam inhibitor resulting in lower carbapenem MICs (not used as independent anti-TB agent).
Cross-resistance	None reported.
Dose	Doses are empiric: randomized clinical trials have not been performed. **Adults:** 125 mg of clavulanate given 30-60 minutes before each dose of carbapenem (2x or 3x/day); avoid extended-release formulations. **Children:** 13 mg/kg as the amoxicillin component before each dose of carbapenem. Maximum dose 500 mg. See **Chapter 6, *Pediatrics*** for weight-based dosing tables. Note: This dose is based on Shah et al., 2022. Sentinel Project 2022, WHO 2022, and ATS/CDC/ERS/IDSA 2019 recommend higher doses. **Renal failure:** Consider twice daily; for creatinine clearance < 10 ml/min, consider once daily. **Hemodialysis:** Single dose every 24 hours and after each dialysis session.
Route of administration	Oral, only to be used with a carbapenem (e.g., imipenem/cilastatin or meropenem).
Preparation	Multiple oral suspension and tablet formulations; common formulations that might be used include amoxicillin 500 mg and clavulanate potassium 125 mg (tablet), amoxicillin 875 mg and clavulanate potassium 125 mg (tablet), and amoxicillin 250 mg and clavulanate potassium 52.5 mg per 5 mL (suspension). Avoid extended-release formulations.
Storage	Tablets are stable at room temperature; reconstituted suspension should be stored in the refrigerator and discarded after 10 days.
Pharmacokinetics	Time to peak oral concentration is 1-1.5 hours. **Half-life** (for clavulanic acid; see amoxicillin nomogram for amoxicillin clearance): about 1 hour
Oral absorption	Good oral absorption, best tolerated and well absorbed when taken at the start of a standard meal.
CSF penetration	Approximately 5% of the plasma concentration reaches the CSF.
Special circumstances	**Use in pregnancy/breastfeeding:** Probably safe in pregnancy (no known risk); can be used while breastfeeding. **Use in renal disease:** Amoxicillin is renally excreted and the dose should be adjusted for renal failure. It is cleared by hemodialysis, so should be dosed after dialysis (see above). Consider using the formulation that offers the lowest amoxicillin dose. **Use in hepatic disease:** Clavulanate is cleared by the liver, so care should be taken when using in patients with liver failure. Amoxicillin/clavulanate is among the most common causes of clinically apparent drug-induced acute liver injury.

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AMOXICILLIN/CLAVULANATE (AMX/CLV) [2 of 2]

Adverse reactions	• Diarrhea (including *C. difficile*), abdominal discomfort common • Hepatotoxicity • Nausea, vomiting, and rash are also common. • Rare side effects have been reported in all other organ systems; rare hypersensitivity is also possible.
Contraindications	Penicillin allergy; use with caution with cephalosporin allergies.
Monitoring	No specific monitoring is required. Consider monitoring transaminases especially in patients with underlying hepatic disease.
2022 wholesale cost 30-day supply, 60-kg person	$29 (outpatient public health pricing, 340B)
Patient instructions	Take at the beginning of a meal. Store tablets at room temperature; store suspension in the refrigerator—throw away after 10 days and refill the prescription. **Call your doctor right away if you have:** • Nausea, vomiting, reduced appetite • Severe diarrhea • Light-colored bowel movements, dark-colored urine, yellowing of your skin or the white of your eyes • Rash • Swelling of the face, hands, feet, or throat

BEDAQUILINE (BDQ) [1 of 2]

Drug class	Diarylquinoline
Trade name	Sirturo
Activity against TB	**Bactericidal;** has strong anti-TB activity. Inhibits adenosine 5'-triphosphate (ATP) synthase with *in vitro* activity against both replicating and nonreplicating bacilli.
Cross-resistance	Cross-resistance with clofazimine has been demonstrated in both directions through efflux-based resistance.
Dose	**Adults:** 400 mg daily for 14 days, followed by 200 mg 3x/week for 22 weeks. FDA approved for 24 weeks* Limited, but growing, clinical experience past 24 weeks of administration. **Children:** [Sentinel Project 2022, WHO 2022] See **Chapter 6, *Pediatrics*** for detailed dosing recommendations. **Renal failure:** No dose adjustment needed for mild to moderate renal insufficiency but should be used with caution in patients requiring renal dialysis. **Concomitant medications:** Bedaquiline is metabolized by CYP3A4 and co-administration of rifamycins (e.g., rifampin, rifapentine and rifabutin) or other strong CYP3A4 inducers may require dose adjustment. See Section 7 in http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/204384s000lbl.pdf. * Note: FDA approval for BPaL is 26 weeks; at least one recent clinical trial of the BPaL regimen used BDQ 200 mg daily for 8 weeks, followed by 100 mg daily for 18 weeks (total 26 weeks).
Route of administration	Oral.
Preparation	20 mg and 100 mg tablets.
Storage	Store at room temperature. Tablets removed from the original packaging should be stored in a tight, light-resistant container and labeled with an expiration date not to exceed 3 months.
Pharmacokinetics	**Peak oral absorption** occurs approximately 5 hours post dose. Administration with a standard meal increases bioavailability about 2-fold, therefore drug should be taken with food. The drug is highly protein-bound. Bedaquiline has a mean terminal half-life of 5.5 months. This likely reflects slow release from peripheral tissues. **Peak concentrations** typically occur 5-6 hours after the dose is given. The typical peak serum or plasma concentration of bedaquiline is 2.8 to 3.3 mcg/mL at week 2 (loading phase), approximately 1.7 mcg/mL at week 8 (maintenance phase), and approximately 1.3 mcg/mL at week 24 (maintenance phase). **Trough concentrations** are typically 0.73 to 0.96 mcg/mL at week 2 (24-hour sample), approximately 0.62 mcg/mL at week 8 (48-hour sample), and approximately 0.36 mcg/mL at week 24 (48-hour sample). **Blood sampling times:** trough, 2 and 5-6 hours post dose. Threshold for dose adjustment remains to be determined. **Half-life:** Terminal about 5.5 months
Oral absorption	Good oral absorption. Should be given with a meal to increase bioavailability.

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BEDAQUILINE (BDQ) [2 of 2]

CSF penetration	Limited data available; BDQ was not detected in CSF of one patient with CNS TB but penetrated freely into the CSF in seven participants with intact blood-brain barriers. Brain concentrations may exceed CSF concentrations. Also, there are no data on the treatment of extrapulmonary TB with BDQ.
Special circumstances	**Use in pregnancy/breastfeeding:** Pregnancy category B. No fetal harm found in animal studies. Limited human data suggest lack of fetal harm within 1-2 years of follow up. The drug is concentrated in breast milk. **Use in renal disease:** No dose adjustment needed for mild to moderate renal insufficiency but should be used with caution in patients requiring peritoneal or hemodialysis. Drug level monitoring may be useful, once available. **Use in hepatic disease:** No dose adjustment is necessary for bedaquiline in patients with mild or moderate hepatic impairment. Bedaquiline has not been studied in patients with severe hepatic impairment and should be used with caution in these patients, and only when the benefits outweigh the risks. Clinical monitoring for bedaquiline -related adverse reactions is recommended.
Adverse reactions	• QTc prolongation • hepatitis • nausea • joint pain • headache • elevated amylase • hemoptysis • chest pain • loss of appetite • rash
Contraindications	None, but use with caution if other QTc prolonging agents, such as clofazimine or fluoroquinolones, are being given.
Monitoring	ECG at baseline, 2, 12 and 24 weeks of treatment. If on another QTc-prolonging drug, such as clofazimine or fluoroquinolone, CDC recommends weekly ECGs but some experts perform ECGs monthly. Stop bedaquiline if QTc > 500 (confirmed on a second ECG 30 minutes later) and monitor ECGs frequently until QTc returns to normal. Check baseline potassium, calcium and magnesium; repeat electrolyte check if QTc prolongation occurs. Baseline and monthly LFTs.
Warning	Despite FDA black box warning about increased risk of death, bedaquiline is now a prioritized drug in U.S. and WHO guidelines for treatment of drug-resistant TB. Black box warning was based on increased risk of death in the bedaquiline treatment group compared to the placebo treatment group in one placebo-controlled trial; there was no pattern to the cause of death, and cause and effect could not be established. Additional observational and clinical trial data have not found increased cardiac deaths. QTc prolongation can occur with bedaquiline. Use with drugs that prolong the QTc interval may cause additive QTc prolongation.
2022 wholesale cost 24-week supply, 60-kg person	$22,839 (outpatient public health pricing, 340B) Note: BDQ 340B pricing is for 24-week supply; a 26-week supply is recommended if using BPaL/BPaLM regimen.
Patient instructions	Avoid alcohol. Take medication with food. **Call your doctor and stop the medicine right away if you have:** • A fast or irregular heartbeat or if you faint • Nausea, vomiting, abdominal pain, or reduced appetite • Light-colored bowel movements, dark-colored urine, yellowing of your skin or the white of your eyes

CLOFAZIMINE (CFZ) [1 of 2]

Drug class	Iminophenazine
Trade name	Lamprene
Activity against TB	*In vitro* activity against *M. tuberculosis* without much *in vivo* data.
Cross-resistance	Bedaquiline. Cross-resistance has been reported in both directions through efflux-based resistance.
Dose	**Adults:** 100 mg daily (oral) **Children:** [Sentinel Project 2022, ATS/CDC/ERS/IDSA 2019] 2-5 mg/kg/day **Renal failure:** No adjustment required.
Route of administration	Oral; not available parenterally.
Preparation	50 and 100 mg capsules.
Storage	Room temperature.
Pharmacokinetics	**Peak oral absorption** occurs at 4–8 hours when given with food. **Peak concentrations** 2–3 hours after a dose are expected to be 0.5 – 2.0 mcg/mL. **Blood sampling times**: 2 and 6 hours post dose. **Half-life** in tissue estimated to be around 70 days.
Oral absorption	70% absorption after an oral dose.
CSF penetration	Limited data are available regarding CNS penetration.
Special circumstances	**Use in pregnancy/breastfeeding:** Not recommended due to limited data (some reports of normal outcomes, some reports of neonatal deaths). Avoided with breastfeeding due to pigmentation of the infant. **Use in renal disease:** No dosage adjustment required. **Use in hepatic disease:** Partially metabolized by the liver; use caution and/or adjust the dose for severe hepatic insufficiency.
Adverse reactions	• Orange-pink, red, or brownish-black discoloration of skin, conjunctiva, cornea, and body fluids. Depression has been reported in response to skin changes. • Gastrointestinal intolerance (crystal deposition in intestinal mucosa, spleen, and liver). • Photosensitivity • QT prolongation (risk for torsades de pointes) if >100 mg/day or in combination with other QT prolonging drugs • Other side effects include retinopathy, dry skin, pruritus, rash, ichthyosis, and severe abdominal symptoms, GI bleeding, and bowel obstruction.
Contraindications	**Allergy to clofazimine.**

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CLOFAZIMINE (CFZ) [2 of 2]

Monitoring	Symptomatic monitoring for skin and GI issues. Consider ECG at baseline and at least monthly if used in combination with other QT prolonging drugs. Clofazimine is not commercially available within the United States. Clinicians should contact the FDA's Office of Emergency Operations (866-300-4374 or 301-796-8240 or DAIP.EIND.SPIND.REQUESTS@fda.hhs.gov) to apply for a single patient Investigational New Drug (IND). The drug is made available on a case-by-case basis without charge. Some state health departments or TB Centers of Excellence have IRB protocols to support acquisition of clofazimine.
Patient instructions	Take with food to avoid stomach upset and improve absorption. This medicine may discolor your skin and body secretions orange-pink, red, or brownish-black. This should go away after stopping the medicine but may take a long time. Avoid the sun and use strong sunscreens. **Call your doctor right away if you have:** • Discoloration of your skin or eyes • Nausea, vomiting, or abdominal pain • Depression or thoughts of hurting yourself • A fast or irregular heartbeat or if you faint

CYCLOSERINE (CS) [1 of 2]

Drug class	Analog of D-alanine
Trade name	Seromycin
Activity against TB	**Bacteriostatic;** inhibits cell wall synthesis.
Cross-resistance	None reported.
Dose	**Adults:** Usually 250 to 750 mg/day in 1 or 2 divided doses to achieve 20-35 mg/L in plasma. Consider dose ramping strategy of 250 mg once daily for 3-4 days, 250 mg twice daily for 3-4 days, then 250 in the morning and 500 mg in the evening. **Children:** [Sentinel Project 2022, ATS/CDC/ERS/IDSA 2019] 15-20 mg/kg/day (max 1000 mg/day) Note: AAP suggests dividing into 2 daily doses **Vitamin B6:** Although there are little supporting data, many MDR-TB experts recommend that patients should receive vitamin B6 while taking cycloserine to prevent neurologic adverse events. Adults often receive 100 mg and children should receive a dose proportionate to their weight. **Renal failure:** 250 mg once daily or 500 mg 3x/week; monitor drug concentrations to keep peak concentrations < 35 mcg/mL. See **Chapter 7, *Co-morbidities and Special Situations – Renal Failure.***
Route of administration	Oral; not available parenterally.
Preparation	250 mg capsule.
Storage	Room temperature in airtight containers.
Pharmacokinetics	**Peak oral absorption** usually occurs by 2 hours (may be up to 4 hours). **Peak concentrations** are expected to be between 20 and 35 mcg /mL. CNS toxicity is associated with concentrations over 35 mcg/mL but may occur even at lower concentrations. Some MDR clinicians prefer to keep the peak concentration <30 mcg/mL. **Blood sampling times** 2 and 6 hours post dose. **Half-life** 8-10 hours with normal renal function
Oral absorption	Modestly decreased by food (best to take on an empty stomach)
CSF penetration	Concentrations approach those in serum.
Special circumstances	**Use in pregnancy/breastfeeding:** Not well studied, but no teratogenicity documented. Use if there are not better choices. Can be used while breastfeeding (dose the infant with vitamin B6 if breastfed). **Use in renal disease:** Cycloserine is cleared by the kidney and requires dose adjustment for renal failure (see above). Use with caution. **Use in hepatic disease:** Not associated with hepatotoxicity.

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CYCLOSERINE (CS) [2 of 2]

Adverse reactions	CNS toxicity, including inability to concentrate and lethargy. More serious CNS side effects, including seizure, depression, psychosis, and suicidal ideation, *usually* occur at peak concentrations > 35 mcg/mL, but may be seen in the normal therapeutic range. Other side effects include peripheral neuropathy and skin changes. Skin problems include lichenoid eruptions and Stevens-Johnson syndrome.
Contraindications	**Significant CNS disease,** including seizure disorder, depression, severe anxiety, psychotic disease, or excessive concurrent use of alcohol. Package insert also lists severe renal insufficiency.
Monitoring	Peak concentrations should be obtained within the first 1–2 weeks of therapy and monitored serially during therapy. The peak concentration should be kept below 35 mcg/mL. Baseline and monthly monitoring for depression using a tool such as the PHQ9 or Beck Depression Index should be done.
2022 wholesale cost 30-day supply, 60-kg person	$269 (outpatient public health pricing, 340B)
Patient instructions	Best taken on an empty stomach. If food is taken, avoid a large fatty meal. Avoid alcohol. Your doctor may also ask you to take a vitamin B6 supplement while on this drug. **Call your doctor right away if you have:** • Seizures • Shakiness or trouble talking • Depression or thoughts of hurting yourself • Anxiety, confusion, or loss of memory • Personality changes, such as aggressive behavior • Rash or hives • Headache

DELAMANID (DLM) [1 of 2]

Drug class	Nitroimidazo-oxazole derivative
Trade name	Deltyba (in Europe)
Activity against TB	**Bactericidal;** has strong anti-TB activity. Inhibits mycolic acid biosynthesis.
Cross-resistance	Cross-resistance with pretomanid, also a Nitroimidazole.
Dose	**Adults:** 100 mg twice daily with food (EMA approved for 24 weeks). Limited clinical experience beyond 24 weeks of administration. **Children:** [Sentinel Project 2022, WHO 2022] < 3 mo of age: 25 mg daily > 3 mo of age up to 16 kg: 25 mg twice daily 16-29.9 kg: 50 mg every morning, 25 mg nightly 30 – 49.9 kg: 50 mg twice daily ≥ 50 kg: 100 mg twice daily with food See **Chapter 6, *Pediatrics*** for weight-based dosing table. **Renal failure:** No dose adjustment needed for mild to moderate renal insufficiency but there are no data regarding use in patients with severe renal impairment. Therefore, delamanid is not recommended for patients with severe renal impairment.
Route of administration	Oral.
Preparation	50 mg film coated tablets.
Storage	Store at room temperature and in original package to protect from moisture.
Pharmacokinetics	**Time of peak oral absorption** (T_{max}) occurs approximately 4 hours post dose. Administration with a standard meal increases bioavailability about 3-fold, therefore drug should be taken with food. The drug is highly protein-bound and displays a large volume of distribution. **Peak concentrations** (C_{max}) at steady state (approximately 14 days of administration) were 369 and 361 mg/mL after the first and second dose, respectively (0.37 and 0.36 mcg/mL). **Half-life** 30 to 38 hours.
Oral absorption	25-47% of the delamanid dose is absorbed following oral administration with food.
Metabolism	The drug is predominantly metabolized in plasma by albumin. Minimal metabolism of delamanid also occurs in human liver microsomes by cytochrome P450 (CYP) 3A4.
CSF penetration	No data are available. Also, there are no data on the treatment of extrapulmonary TB (e.g., central nervous system, bone) with delamanid.

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DELAMANID (DLM) [2 of 2]

Special circumstances	**Use in pregnancy/breastfeeding:** Delamanid may cause harm to a fetus. It is usually not recommended for use during pregnancy. It is not known if delamanid passes into breast milk in humans. Breastfeeding is not recommended during treatment with delamanid. **Use in renal disease:** No dose adjustment needed for mild to moderate renal insufficiency, but delamanid is not recommended for patients with severe renal impairment. **Use in hepatic disease:** No dose adjustment is necessary for delamanid in patients with mild hepatic impairment, but it is not recommended in patients with moderate to severe hepatic impairment. Delamanid is contraindicated in patients with serum albumin levels <2.8 g/mL.
Adverse reactions	The most frequent adverse drug reactions noted in controlled trials using delamanid with background regimens were nausea, vomiting, dizziness, insomnia, and upper abdominal pain. QTc prolongation occurred in about 10% of patients receiving 100 mg twice daily. However, no episodes were accompanied by clinical symptoms such as arrhythmias or syncope.
Contraindications	• Hypersensitivity to delamanid • Serum albumin < 2.8 g/mL because of an increased risk of QTc prolongation • Taking other medications that are strong inducers of CYP3A (e.g., carbamazepine, rifamycins)
Monitoring	ECG at baseline and monthly during treatment. Baseline electrolytes, repeat if QTc prolongation occurs.
2022 wholesale cost 24-week supply, 60-kg person	Not available [Has been obtained in U.S. under manufacturer's compassionate use program.] Contact Otsuka (Medical@otsuka-onpg.com), CDC, your state TB control program, and your CDC TB Center of Excellence to help expedite the process.
Patient instructions	Take medication with food **Call your doctor and stop the medicine right away if you have:** • A fast or irregular heartbeat or if you faint • Nausea, vomiting, abdominal pain, or reduced appetite

ETHAMBUTOL (EMB, E) [1 of 2]

Drug class	Ethylenediamine
Trade name	Myambutol
Activity against TB	**Bacteriostatic** inhibitor of cell wall synthesis; bactericidal only at the high end of the dosing range. At doses used over long periods of time, ethambutol protects against further development of resistance.
Cross-resistance	None reported.
Dose	**Adults:** 15–25 mg/kg/day. For drug-resistant TB, MDR clinicians often start patients at 25 mg/kg dosing, then drop to 15 mg/kg dosing after two months to avoid toxicity. **Children:** [Sentinel Project 2022, WHO 2022, AAP 2021] 15-25 mg/kg/day (max 1000 mg/day). **Renal failure:** 15–25 mg/kg/dose 3x/weekly (not daily). **Obesity:** Serum concentrations should be monitored, as dosing with lean body weight likely will lead to under-dosing.
Route of administration	Oral; not available parenterally in the U.S.
Preparation	100 mg tablets; scored 400 mg tablets; coated 100 mg tablets; coated, scored 400 mg tablets.
Storage	Room temperature.
Pharmacokinetics	**Peak oral absorption** occurs 2–4 hours after the dose. **Peak concentrations** of 2– 6 mcg/mL are expected with daily dosing. **Blood sampling times:** 2 and 6 hours post dose. **Half-life** (normal renal function): 2 to 4 hours, with low concentrations remaining longer.
Oral absorption	80% bioavailability independent of food.
CSF penetration	Ethambutol penetrates meninges poorly.
Special circumstances	**Use in pregnancy/breastfeeding:** Safe in pregnancy; can be used while breastfeeding. **Use in renal disease:** Use with caution—cleared by the kidneys; dose adjustment required for renal failure. Increased risk of toxicity with renal failure. If needed for use in the regimen, consider therapeutic drug monitoring. See **Chapter 7, *Co-morbidities and Special Situations — Renal Failure.*** **Use in hepatic disease:** Safe in liver disease.
Adverse reactions	Retrobulbar neuritis (dose-related—exacerbated during renal failure).
Contraindications	**Pre-existing optic neuritis; visual changes on ethambutol.**

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ETHAMBUTOL (EMB, E) [2 of 2]

Monitoring	Patients should be counseled to report any changes in vision. Baseline and monthly visual acuity and color discrimination monitoring should be performed (particular attention should be given to individuals on higher doses or with renal impairment).
2022 wholesale cost 30-day supply, 60-kg person	$23 (outpatient public health pricing, 340B)
Patient instructions	Can be taken with food or on an empty stomach. **Call your doctor right away if you have:** • Any problems with your eyes: vision changes, blurring, color blindness, trouble seeing, or eye pain

ETHIONAMIDE (ETA, ETO) [1 of 2]

Drug class	Derivative of isonicotinic acid
Trade name	Trecator-SC
Activity against TB	**Weakly bactericidal;** blocks mycolic acid synthesis.
Cross-resistance	Cross-resistance to isoniazid may occur when there is low-level resistance to ethionamide due to mutation in *inhA* or the promoter region.
Dose	**Adults:** 15–20 mg/kg/day, often divided twice daily; usually 500–750 mg total per day in 2 divided doses. Most patients will experience GI intolerance with ETA doses greater than 1000 mg daily. Consider dose ramping strategy to support early tolerability (see **Chapter 4, *Treatment – Drug Ramping)***. **Children:** [Sentinel Project 2022, WHO 2022, AAP 2021, ATS/CDC/ERS/IDSA 2019] 15-20 mg/kg/day (max 1000 mg/day); guidelines suggest daily or divided into 2 or 3 daily doses **Vitamin B6:** Although there are little supporting data, many MDR-TB experts recommend that all patients should receive vitamin B6 to prevent peripheral neuropathy while taking ethionamide. Adults often receive 100 mg and children should receive a dose proportionate to their weight. **Renal failure:** No change.
Route of administration	Oral; not available parenterally.
Preparation	Coated 250 mg tablet.
Storage	Store at room temperature.
Pharmacokinetics	**Peak oral absorption** is usually reached in 2–3 hours, but delayed absorption is common. **Peak concentrations** are typically 1–5 mcg/mL. **Blood sampling times** 2 and 6 hours post dose. **Half-life** 2 hours
Oral absorption	Erratic absorption, possibly due to GI disturbances associated with the medication.
CSF penetration	Concentrations approach those in serum; one pediatric study evaluating drug concentrations in the CSF suggests that ethionamide should be dosed on the high end of the range for patients with meningitis.
Special circumstances	**Use in pregnancy/breastfeeding:** Generally avoided during pregnancy due to reports of teratogenicity; little data about use during breastfeeding—an estimated 20% of a usual therapeutic dose is thought be received (dose the infant with vitamin B6 if breastfed). **Use in renal disease:** No precautions are required for renal impairment. **Use in hepatic disease:** Can cause hepatotoxicity similar to that of INH—use with caution in liver disease.

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ETHIONAMIDE (ETA, ETO) [2 of 2]

Adverse reactions	• Gastrointestinal upset and anorexia: Sometimes intolerable (symptoms are moderated by food or taking at bedtime). Premedication with an antiemetic like ondansetron is often helpful. Low dose lorazepam 0.5 mg has also been used successfully. • Metallic taste. • Hepatotoxicity • Depression • Endocrine effects: Gynecomastia, hair loss, acne, impotence, menstrual irregularity, and reversible hypothyroidism—treat with thyroid replacement. • Neurotoxicity: Side effects may be exaggerated in patients also taking cycloserine.
Contraindications	**Sensitivity to ethionamide.**
Monitoring	Monitor TSH (consider baseline and every 3 months) for evidence of hypothyroidism requiring replacement; therapeutic drug monitoring if malabsorption suspected. Monitor liver function tests.
2022 wholesale cost 30-day supply, 60-kg person	$188 (outpatient public health pricing, 340B)
Patient instructions	Take this medicine with food. Your doctor may also ask you to take a high-dose vitamin B6 supplement while on this drug. **Call your doctor right away if you have:** • Depression or thoughts of hurting yourself • Anxiety, confusion, or loss of memory • Personality changes, such as aggressive behavior • Dizziness • Nausea, vomiting, abdominal pain, or reduced appetite • Light-colored bowel movements, dark-colored urine, yellowing of your skin or the white of your eyes • Swollen breasts (in men)

IMIPENEM /CILASTATIN (IMP/CLN) [1 of 2]

Drug class	Beta-lactam – carbapenem
Trade name	Primaxin
Activity against TB	**Bactericidal:** *In vitro* activity.
Cross-resistance	Imipenem and Meropenem are both carbapenems and likely to have a moderate probability of cross-resistance.
Dose	**Adults:** 1000 mg IV every 8-12 hours. Administer with clavulanate given 30-60 minutes before each dose of carbapenem (see Amoxicillin/clavulanate medication fact sheet for dosage) **Children:** Not currently recommended for pediatrics (seizure risks). **Renal failure:** Adjustment in dose based on severity of renal failure —for example, 750-1000 mg every 12 hours for creatinine clearance 20–40 mL/min, 500-750 mg every 12 hours for creatinine clearance < 20 mL/min. Monitor concentrations where available. Administer with clavulanate given 30-60 minutes before each dose of carbapenem. See ***Amoxicillin/clavulanate*** for dosage.
Route of administration	IV or IM (total IM doses are not recommended more than 1500 mg/day and are therefore not very practical for treatment of drug-resistant TB). No oral preparation.
Preparation	Lypholized powder 1:1 ratio of imipenem and cilastatin. Vials are available 250, 500, 750 mg or 1000 mg.
Storage	Powder should be kept at room temperature; suspended product should be kept no more than 4 hours at room temperature or no more than 24 hours refrigerated.
Pharmacokinetics	**Peak concentrations** (35-60mcg/mL for a 1000 mg infusion) occur immediately after IV infusion and 1 hour after IM injection. **Blood sampling times:** trough and 1 hour post dose. **Half-life** (normal renal function) 1 hour
Oral absorption	No oral absorption.
CSF penetration	Good CSF penetration, but children with meningitis treated with imipenem had high rates of seizures (meropenem preferred for meningitis and for children).
Special circumstances	**Use in pregnancy/breastfeeding:** Little information known regarding use in pregnancy; unknown safety during breastfeeding. **Use in renal disease:** Dose adjustment required (see above); dose after hemodialysis. **Use in hepatic disease:** Elevated liver function tests have been noted in up to 6% of patients, but no definite liver damage has been documented.
Adverse reactions	• Diarrhea (including *C. Difficile*), nausea, or vomiting. • Seizure. • Decreased hematocrit, eosinophilia, thrombocytopenia, as well as increased AST, common in infants and children.
Contraindications	**Carbapenem intolerance; meningitis** (use meropenem rather than imipenem).

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IMIPENEM /CILASTATIN (IMP/CLN) [2 of 2]

Monitoring	Symptomatic monitoring.
2022 wholesale cost 30-day supply, 60-kg person	$572 (outpatient public health pricing, 340B)
Patient instructions	Make sure your doctor knows if you are also taking ganciclovir or have allergy to penicillin or cephalosporins. **Call your doctor right away if you have:** • Severe diarrhea (watery or bloody) • Nausea, vomiting, or reduced appetite • Seizures

ISONIAZID (INH, H) [1 of 2]

Drug class	Isonicotinic acid hydrazide
Trade name	INH/Isoniazid/Laniazid/Nydrazid
Activity against TB	**Bactericidal,** especially for rapidly dividing cells. Affects mycolic acid (cell wall) synthesis.
Cross-resistance	Cross-resistance to ethionamide may occur when there is low-level resistance to isoniazid due to a mutation in *inhA* or the promoter region.
Dose	**Adults:** 5 mg/kg/day (PO or IV) usual adult dose 300 mg daily; high-dose INH (900 to 1500 mg 2x/week or 3x/week) is sometimes used, especially for patients with low-level INH resistance. **Children:** [Sentinel Project 2022, WHO 2022, ATS/CDC/ERS/IDSA 2019] 10-15 mg/kg/day (max 300 mg) standard dose or 20–30mg/kg/dose 2x/week or 3x/week 15-20 mg/kg (high dose, consider when low-level INH resistance) **Renal failure:** No adjustment required. **Vitamin B6** (25-50mg) should be used in patients with diabetes, uremia, HIV infection, alcohol abuse, malnutrition, or peripheral neuropathy and in all patients on high-dose INH in order to decrease risk of peripheral neuropathy. Additionally, pregnant and post-partum women and exclusively breastfeeding infants should receive vitamin B6 while taking INH.
Route of administration	Oral, intravenous, or intramuscular.
Preparation	50 mg, 100 mg, or 300 mg scored or unscored tablets; 50 mg/5 mL oral suspension in sorbitol; solution for injection 100 mg/mL. When given IV, dilute in 25 mL normal saline and infuse as a slow bolus over 5 minutes. Since compatibility information is not available, do not infuse "piggyback" with other drugs through a shared IV line.
Storage	Suspension must be kept at room temperature.
Pharmacokinetics	**Peak serum concentrations** are achieved at 1–2 hours after the oral dose. **Peak concentration** is expected to be 3–5 mcg/mL after daily dose and 9–15 mcg/mL after twice weekly dose. **Blood sampling times:** 2 and 6 hours post dose. **Half-life (may be prolonged in patients with impaired hepatic or renal function)** Fast acetylators 30-100 minutes (by definition <2 hours), slow acetylators 2-4 hours
Oral absorption	Well absorbed orally or intramuscularly; best absorbed on an empty stomach; up to 50% reduction in peak concentration with a fatty meal.
CSF penetration	Concentration equivalent to plasma in inflamed meninges. 20% of concentrations in plasma in non-inflamed meninges.

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ISONIAZID (INH, H) [2 of 2]

Special circumstances	**Use in pregnancy/breastfeeding:** Safe during pregnancy; safe during breastfeeding (mother should receive pyridoxine supplementation). Up to 20% of the infant therapeutic dose will be passed to the baby in the breast milk. **Use in renal disease:** No dose adjustment for renal failure, but pyridoxine supplementation should be used. **Use in hepatic disease:** May exacerbate liver failure. Use with caution. **Drug interactions:** Isoniazid is a CYP3A4 inhibitor. INH may increase the concentrations of certain cytochrome P450 enzyme substrates, including phenytoin and carbamazepine.
Adverse reactions	• Mild, transient increase in serum transaminases is common. • Hepatitis (age-related). • Peripheral neuropathy. • Other reactions, including optic neuritis, arthralgias, CNS changes, drug-induced lupus, diarrhea, DRESS or hypersensitivity reaction, and seizures. • The liquid formulation contains sorbitol and can cause abdominal cramping.
Contraindications	Hypersensitivity or drug-induced hepatitis due to isoniazid; avoid if acute liver failure.
Monitoring	**Clinical monitoring of all patients on INH is essential.** Routine laboratory monitoring is recommended for certain patients receiving INH monotherapy. For patients receiving multiple TB drugs or other hepatotoxic drugs, with underlying liver disease (including viral hepatitis), or who are pregnant, baseline liver function testing is recommended. Follow-up liver function testing is determined by baseline concerns and symptoms of hepatotoxicity. Monitor concentrations of phenytoin or carbamazepine in patients receiving those drugs (increases phenytoin concentrations and risk of hepatotoxicity with carbamazepine), especially when undergoing INH monotherapy. Rifampin tends to lower concentrations of these drugs and balance effect of INH.
2022 wholesale cost 30-day supply, 60-kg person	$2 (outpatient public health pricing, 340B)
Patient instructions	Do not take this medication with a large fatty meal. If you have an upset stomach, take the medicine with a snack. If you (or your child) are taking the liquid suspension—do not put it in the refrigerator. Avoid alcohol while taking this medicine. If you need an antacid, don't take it within 1 hour of this medicine. Make sure your doctor knows if you are also taking medicine for seizures. Let your doctor know if you get flushing, sweating, or headaches when eating certain cheeses or fish. Ask your doctor if you should be taking a vitamin B6 (pyridoxine supplement). **Call your doctor right away if you have any of these side effects:** • Loss of appetite for a few days that is not going away • Tiredness, weakness • Moderate stomach pain, nausea, or vomiting • Numbness or tingling of your fingers or toes • Blurred vision, eye pain • Yellow skin or eyes or dark-colored urine

LEVOFLOXACIN (LFX) [1 of 2]

Drug class	Fluoroquinolone
Trade name	Levaquin
Activity against TB	**Bactericidal;** has strong anti-TB activity. Greater activity than ciprofloxacin or ofloxacin. Inhibits DNA gyrase.
Cross-resistance	In general, there is a complete class effect cross-resistance among fluoroquinolones *in vitro*. However, data suggest that moxifloxacin may continue to demonstrate some activity despite *in vitro* resistance to ofloxacin.
Dose	**Adults:** For treatment of TB disease: 750–1000 mg/day (PO or IV). **Children:** [Sentinal Project 2022, WHO 2022, AAP 2021, ATS/CDC/ERS/IDSA 2019] 15-20 mg/kg/day (max 1000 mg/day) **Renal failure:** 750–1000 mg/dose 3x/week (not daily) for creatinine clearance < 50 ml/min. Moxifloxacin may be preferred in renal failure.
Route of administration	Oral or intravenous.
Preparation	Coated tablets (250 mg, 500 mg, 750 mg); solution for injection 25 mg/mL; 250 mg in 50 mL container; 500 mg in 100 mL container; 750 mg in 150 mL container. Oral suspension is 25 mg/mL.
Storage	Oral forms, undiluted solution, and pre-mixed solutions are stored at room temperature. Once diluted, the solution can be kept at room temperature for 3 days, in the refrigerator for 2 weeks, or frozen for 6 months.
Pharmacokinetics	**Peak oral absorption** occurs at 1–2 hours. **Peak concentrations** of 8 –12 mcg/mL are expected. **Blood sampling times:** 2 and 6 hours post dose. **Half-life** (adult, normal renal function): 6-8 hours.
Oral absorption	Excellent oral absorption. Should not be administered by mouth within 2 hours of ingestion of milk-based products, antacids, or other medications containing divalent cations (iron, magnesium, calcium, zinc, vitamins, didanosine, sucralfate).
CSF penetration	Concentrations are 65% of that in the serum.
Special circumstances	**Use in pregnancy/breastfeeding:** Fluoroquinolones are generally avoided in pregnancy and breastfeeding due to observation of arthropathy in puppy models. However observational data suggest that fluoroquinolone exposure, even in the first trimester, is not associated with adverse fetal outcomes. **Use in renal disease:** Dosage adjustment is recommended if creatinine clearance is < 50 mL/min per package insert. The drug is not cleared by hemodialysis; supplemental doses after dialysis are not necessary. **Use in hepatic disease:** Drug concentrations not affected by hepatic disease. Presumed to be safe in severe liver disease. Consider monitoring LFTs. Rarely associated with hepatotoxicity in case reports.

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LEVOFLOXACIN (LFX) [2 of 2]

Adverse reactions	• Nausea and bloating • Headache, dizziness, insomnia, or tremulousness • Tendonitis and rare tendon rupture (increased risk >60 years old or with corticosteroid use), arthralgias (can usually be treated symptomatically) • QTc prolongation, hypoglycemia • Hypersensitivity • Antibiotic-associated diarrhea or *C. difficile* colitis • Aortic aneurysm and aortic dissection (older age, peripheral vascular disease, prior aneurysm increase risk)
Contraindications	**Fluoroquinolone intolerance, prolonged QTc, pregnancy (relative contraindication)**
Monitoring	Side effect monitoring, but no specific laboratory monitoring required.
2022 wholesale cost 30-day supply, 60-kg person	$4 (outpatient public health pricing, 340B)
Patient instructions	You can take levofloxacin with food. Drink plenty of beverages. Do not take milk-based products, antacids (especially aluminum-containing), mineral supplements such as iron or magnesium, or multivitamins within 2 hours of this medication. This medicine may cause sun sensitivity; use sunscreens. Do not undertake new strenuous activities. **Call your doctor and stop the medicine right away if you have:** • Pain, swelling or "popping" of a tendon (such as the back of your ankle, elbow, etc.), or muscle or joint pain • Chest pain, trouble breathing, or tightness in your chest • Diarrhea • Headache, trembling, or difficulty sleeping • Anxiety, confusion, or dizziness • Rash • Swelling of the face, hands, feet, or throat

LINEZOLID (LZD) [1 of 2]

Drug class	Oxazolidinones
Trade name	Zyvox
Activity against TB	Has *in vitro* **bactericidal** activity; inhibits protein synthesis.
Cross-resistance	None reported.
Dose	**Adults:** 600 mg once daily. **Children:** [Sentinel Project 2022, WHO 2022] 15 mg/kg (< 16 kg) 10-12 mg/kg (> 16 kg) 300 mg for children 21 kg or more and younger than 12 years.
Route of administration	Oral or intravenous.
Preparation	Coated tablets: 600 mg; intravenous solution: 2 mg/mL: 100-, 200-, or 300-mg bags. Oral powder for suspension: 100 mg/5 mL 240 mL bottle.
Storage	Store tablet at room temperature. Reconstituted oral suspension may be stored at room temperature for 21 days. Parenteral preparation should be stored at room temperature (protect from light and do not freeze).
Pharmacokinetics	Intravenous doses are administered over 30–120 minutes. **Peak concentrations** are achieved 1–1.5 hours after an oral dose and ½ hour after an IV dose. **Peak concentrations** are expected to be 12–24 mcg/mL. **BPaL blood sampling times:** trough, 2 and 5-6 hours post dose. **Half-life** (adult, normal renal function): about 3-5 hours
Oral absorption	Nearly complete oral absorption.
CSF penetration	CSF concentrations are about 1/3 of those in serum in animal models, and linezolid has been used to treat meningitis in humans.
Special circumstances	**Use in pregnancy/breastfeeding:** Not recommended during pregnancy or breastfeeding due to limited data. **Use in renal disease:** No dose adjustment is recommended, but metabolites may accumulate. **Use in hepatic disease:** Rarely associated with increased transaminases.
Adverse reactions	• Myelosuppression; thrombocytopenia, anemia, and leukopenia • Diarrhea and nausea, including *C.difficile* colitis • Optic and peripheral neuropathy – most resolve, but can be irreversible • Serotonin syndrome • **Vitamin B6:** Prior expert recommendations suggested use of vitamin B6 while taking LZD. However, the mechanism of toxicity for LZD is unclear and may be associated with mitochondrial toxicity. B6 is not thought to play a role in most LZD-related adverse events and unlikely to have protective benefits.

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LINEZOLID (LZD) [2 of 2]

Contraindications	**Hypersensitivity to oxazolidinones.** **Symptoms of neuropathy** (pain, numbness, tingling or weakness in the extremities). **Drug Interactions:** Linezolid should generally not be administered to patients taking serotonergic agents, such as monoamine oxidase inhibitors (MAOIs) due to the potential for serious CNS reactions, such as serotonin syndrome. Since MAO type A deaminates serotonin, and SSRIs potentiate the action of serotonin by inhibiting its neuronal reuptake, administration of linezolid concurrently with an SSRI can lead to serious reactions such as serotonin syndrome or neuroleptic malignant syndrome-like reactions.
Monitoring	Monitor for peripheral neuropathy and optic neuritis. Monitor CBC weekly during the initial period, then monthly, and then as needed based on symptoms
2022 wholesale cost 30-day supply, 60-kg person	$16 (outpatient public health pricing, 340B)
Patient instructions	This medicine may be taken with or without food. Try taking it with food if it bothers your stomach. Avoid excessive amounts of food and drinks that contain tyramine (aged cheeses, dried meats, sauerkraut, soy sauce, tap beers, and red wines); however, careful tyramine restriction is not needed. Make sure your doctor knows if you're taking medicines for depression. **Call your doctor right away if you have any of these side effects:** • Unusual bleeding or bruising • Pain, numbness, tingling or weakness in the extremities • Severe diarrhea, nausea, or vomiting • Changes in vision • Agitation, confusion, fast or irregular heartbeat, twitching muscles

MEROPENEM (MPM) [1 of 2]

Drug class	Beta-lactam – carbapenem
Trade name	Merrem I.V.
Activity against TB	**Bactericidal:** *In vitro* activity—very limited clinical experience.
Cross-resistance	Meropenem and imipenem are both carbapenems and likely to have a moderate probability of cross-resistance.
Dose	**Adults:** Different doses have been used, usually 1000—2000 mg every 8 hours; WHO recommends 2000 mg every 12 hours. Bactericidal activity may be greater at total daily dosages of 6000 mg daily. Administer with clavulanate given 30-60 minutes before each dose of carbapenem (see ***Amoxicillin/clavulanate*** fact sheet for dosage). **Children:** [Sentinel Project 2022, WHO 2022, ATS/CDC/ERS/IDSA 2019] 20–40 mg/kg every 8 hours; use with clavulanic acid (Sentinel Project suggests giving 30 minutes before carbapenem). **Renal failure:** Adjustment in dose and interval based on severity of renal failure and body weight—for example, 750 mg every 12 hours for creatinine clearance 20-40 mL/min, 500 mg every 12 hours for creatinine clearance < 20 mL/min. Monitor concentrations where available. Administer with clavulanate given 30-60 minutes before each dose of carbapenem (see ***Amoxicillin/clavulanate*** fact sheet for dosage).
Route of administration	IV only; no oral preparation.
Preparation	Crystalline powder. Product is available in 500 mg or 1000 mg vials.
Storage	Powder should be kept at room temperature; suspended product should be kept no more than 4 hours at room temperature or no more than 24 hours refrigerated.
Pharmacokinetics	**Peak concentration:** At the end of a 30-minute infusion, peak concentration after a 1000 mg dose should be 39-58 mcg/mL. **Blood sampling times:** Trough and 1 hour post dose **Half-life** (adult, normal renal function) 1 hour
Oral absorption	No oral absorption.
CSF penetration	Poor CSF penetration; increased dosing and shorter dosing intervals may help mitigate this.
Special circumstances	**Use in pregnancy/breastfeeding:** Little information known regarding use in pregnancy; unknown safety during breastfeeding. **Use in renal disease:** Dose adjustment required (see above); dose after hemodialysis. **Use in hepatic disease:** Liver disease does not alter the pharmacodynamics of meropenem.

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MEROPENEM (MPM) [2 of 2]

Adverse reactions	• Diarrhea, nausea, or vomiting. • Seizure (noted with CNS infection), but rare compared to imipenem. • Rarely elevated LFTs, hematologic toxicity, hypersensitivity
Contraindications	**Carbapenem intolerance**
Monitoring	Symptomatic monitoring.
2022 wholesale cost 30-day supply, 60-kg person	$531 (outpatient public health pricing, 340B)
Patient instructions	Make sure your doctor knows if you have allergy to penicillin or cephalosporins. **Call your doctor right away if you have:** • Severe diarrhea (watery or bloody) • Skin rash, hives, or itching • Swelling in the face, throat, or lips • Wheezing or trouble breathing

MOXIFLOXACIN (MFX) [1 of 2]

Drug class	Fluoroquinolone
Trade name	Avelox
Activity against TB	**Bactericidal;** inhibits DNA gyrase.
Cross-resistance	In general, there is a complete class effect cross-resistance among fluoroquinolones *in vitro*. However, data suggest that moxifloxacin may continue to demonstrate some activity despite *in vitro* resistance to ofloxacin.
Dose	**Adults:** 400 mg once daily (PO or IV). Some patients may require 600-800 mg once daily, based on serum concentrations. **Children:** [Sentinal Project 2022, WHO 2022, ATS/CDC/ERS/IDSA 2019] 10-15 mg/kg/day (max 400 mg) **Renal failure:** No dose adjustment required.
Route of administration	Oral or IV.
Preparation	Tablets (400 mg); aqueous solution (400 mg/250 mL) for IV injection.
Storage	Store oral and IV products at room temperature (do not refrigerate).
Pharmacokinetics	**Peak absorption** after an oral dose is noted in 1–3 hours. **Peak concentrations** are expected to be 3-5 mcg/mL. **Blood sampling times** 2 and 6 hours post dose. **Half-life** (adult, normal renal function): 7-8 hours in TB patients.
Oral absorption	Good oral absorption (90% bioavailable). Should not be administered within 2 hours of ingestion of milk-based products, antacids, or other medications containing divalent cations (iron, magnesium, calcium, zinc, vitamins, didanosine, sucralfate).
CSF penetration	Good penetration in animal model studies.
Special circumstances	**Use in pregnancy/breastfeeding:** Fluoroquinolones are generally avoided in pregnancy and breastfeeding due to observation of arthropathy in puppy models. However observational data suggest that fluroquinolone exposure, even in the first trimester, is not associated with adverse fetal outcomes. **Use in renal disease:** Excretion unchanged in the face of renal failure; no data on effect of dialysis. **Use in hepatic disease:** Rarely associated with hepatotoxicity; use with caution. No dose adjustment required for mild or moderate liver disease.
Adverse reactions	• Nausea and diarrhea. • Headache and dizziness. • **Rare** tendon rupture; arthralgias. • Rare hepatotoxicity. • QTc prolongation, hypo/hyperglycemia. • Antibiotic-associated diarrhea or *C. difficile* colitis

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MOXIFLOXACIN (MFX) [2 of 2]

Contraindications	Fluoroquinolone intolerance, prolonged QTc, pregnancy (relative contraindication).
Monitoring	Symptomatic monitoring.
2022 wholesale cost 30-day supply, 60-kg person	$12 (outpatient public health pricing)
Patient instructions	Keep moxifloxacin at room temperature. Moxifloxacin can be taken with food, but do not take milk-based products, antacids (especially aluminum-coating), vitamin supplements, or sucralfate within 2 hours of this medication. Do not undertake new strenuous activities. **Call your doctor and stop the medicine right away if you have:** • Pain, swelling or tearing of a tendon (such as the back of your ankle, elbow, etc.), or muscle or joint pain • Severe diarrhea • A fast or irregular heartbeat or if you faint • Nausea, vomiting, abdominal pain, or reduced appetite

PARA-AMINOSALICYLATE (PAS) [1 of 2]

Drug class	Salicylic acid – anti-folate
Trade name	PASER
Activity against TB	**Bacteriostatic**
Cross-resistance	None reported.
Dose	**Adults:** 4000 mg, 2 or 3 times daily. Some experts use 6000 mg daily. Consider dose ramping strategy to support early tolerability. See **Chapter 4, *Treatment – Drug Ramping.*** **Children:** [Sentinel Project 2022, WHO 2022, AAP 2021, ATS/CDC/ERS/IDSA 2019] 200-300 mg/kg/day (max 10,000 mg/day); guidelines suggest dividing into 2 to 4 daily doses. **Renal failure:** No change.
Route of administration	Oral; should be given sprinkled on or stirred into mildly acidic food (e.g., yogurt or apple sauce or suspension in a fruit drink). Do not chew or crush the granules, they should be swallowed whole. Not available parenterally in the U.S.
Preparation	4000 mg per packet.
Storage	Packets should be kept in the refrigerator or freezer (but may be kept at room temperature for short periods of time)
Pharmacokinetics	Delayed peak concentration with the PASER formulation (the only product available in the United States) due to its enteric coating and sustained release (1–6 hours). **Peak concentrations** are expected to be 20–60 mcg/mL. **Blood sampling times** 6 hours post dose. **Half-life** (adult, normal renal function): about 1-2 hours
Oral absorption	Incomplete absorption—sometimes requires increased doses to achieve therapeutic concentrations.
CSF penetration	Poorly penetrates the meninges (somewhat better with inflammation).
Special circumstances	**Use in pregnancy/breastfeeding:** Not studied, but no teratogenicity known. There is little data regarding use during breastfeeding. In one patient, the milk concentration was 1 mcg/mL compared to a serum concentration of 70 mcg/mL. **Use in renal disease:** Inactive metabolite is cleared by the kidneys. The package insert says to avoid with severe renal failure. Other authorities believe PAS can be used with caution (no toxicity of metabolite known). **Use in hepatic disease:** Use with caution; 0.5% incidence of hepatotoxicity.
Adverse reactions	• Gastrointestinal distress (less with the PASER formulation than with older preparations). Rare hepatotoxicity (0.5%) associated with premonitory symptoms of rash and fever, and hepatomegaly, lymphadenopathy, leukocytosis, and eosinophilia. Full recovery if recognized. High mortality (21%) reported when not recognized promptly. • Rare agranulocytosis, hemolytic anemia, leukopenia, thrombocytopenia. • Reversible hypothyroidism (increased risk with concomitant use of ethionamide)—treat with thyroid replacement. • Other: pericarditis, rash, hepatitis, optic neuritis.

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PARA-AMINOSALICYLATE (PAS) [2 of 2]

Contraindications	**Pregnancy (relative), hypersensitivity to aminosalicylic acid, end-stage renal disease**
Monitoring	Monitor TSH, electrolytes, blood counts, and liver function tests.
2022 wholesale cost 30-day supply, 60-kg person	$329 (outpatient public health pricing)
Patient instructions	Keep the product in the refrigerator or freezer. Sprinkle granules over applesauce or yogurt or swirl in acidic juices (tomato, grape, grapefruit, cranberry, apple, or orange). Do not chew the granules. Do not use the packet if expanded or if the granules are discolored. Gastrointestinal discomfort and diarrhea usually improve over time. The shells of the granules may be seen in the stool — this is normal. **Call your doctor right away if you have any new symptoms, including:** • Skin rash, severe itching, or hives • Severe abdominal pain, nausea, or vomiting • Unusual tiredness or loss of appetite • Easy bruising or bleeding • Severe fatigue

PRETOMANID (Pa, PMD) [1 of 2]

Drug class	Nitroimidazole derivative
Trade name	Pretomanid tablets
Activity against TB	**Bactericidal;** has strong anti-TB activity including nonreplicating organisms. Inhibits mycolic acid biosynthesis; other effects.
Cross-resistance	Cross-resistance with delamanid.
Dose	**Adults:** 200 mg once daily with food (FDA approved for 26 weeks as part of BPaL regimen). Limited clinical experience past 26 weeks of administration. **Children:** Dose not determined for children aged <15 years. **Renal failure:** No dose adjustment needed for mild to moderate renal insufficiency but there are no data regarding use in patients with severe renal impairment. Therefore, pretomanid is not recommended for patients with severe renal impairment.
Route of administration	Oral
Preparation	200 mg tablets
Storage	Store at room temperature and in original package to protect from moisture.
Pharmacokinetics	**Time of peak oral absorption** (T_{max}) occurs approximately 4-5 hours post dose. Administration with a standard meal increases bioavailability about 3-fold, therefore drug should be taken with food. Pretomanid is highly protein-bound and displays a large volume of distribution. **Peak concentrations:** Peak after a single-dose ranges from 1.4 - 2.6 mcg/mL, and at steady state, about 2.3-4.3 mcg/mL. **Trough concentrations** are about 1.0 - 2.4 mcg/mL. Threshold for dose adjustment remains to be determined. **Blood sampling times** trough, 2 and 5-6 hours post dose. **Half-life** (adult, normal renal function): 16-18 hours.
Oral absorption	Food increases oral absorption.
Metabolism	Pretomanid is metabolized by multiple reductive and oxidative pathways, with CYP3A4 responsible for approximately 20%.
CSF penetration	Limited data suggest low CSF concentrations. Brain tissue penetration may be higher.
Special circumstances	**Use in pregnancy/breastfeeding:** There are no studies or available data on pretomanid use in pregnant women to inform any drug-associated risks. **Use in renal disease:** No dose adjustment for pretomanid needed for mild to moderate renal insufficiency; dosing for patients with severe renal impairment not established. **Use in hepatic disease:** No dose adjustment for pretomanid needed for mild to moderate hepatic insufficiency, dosing for patients with severe hepatic impairment not established.

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PRETOMANID (Pa, PMD) [2 of 2]

Adverse reactions	The most common adverse events observed during pretomanid therapy included peripheral neuropathy, anemia, GI upset, and elevated liver enzymes. Testicular toxicity was observed in mice and rats but not in non-human primates or in humans to date.
Contraindications	Hypersensitivity to pretomanid. Taking other medications that are strong or moderate inducers of CYP3A (e.g., carbamazepine, efavirenz, etravirine, rifamycins).
Monitoring	Obtain an ECG before initiation of treatment, and at least 2, 12, and 24 weeks after starting treatment. Check baseline potassium, calcium, and magnesium; repeat electrolyte check if QTc prolongation occurs. Baseline, 2-week, and then monthly LFTs and CBC.
2022 wholesale cost 24-week supply, 60-kg person	$456 (outpatient public health pricing, 340B)
Patient instructions	Take medication with food. **Tell your doctor if you have one of the following conditions:** • Nausea, vomiting, abdominal pain, or reduced appetite • Light-colored bowel movements, dark-colored urine, yellowing of your skin or the white of your eyes • Pain, numbness, tingling or weakness in the extremities • Easy bruising or bleeding

PYRAZINAMIDE (PZA, Z) [1 of 2]

Drug class	Synthetic derivative of nicotinamide
Trade name	Pyrazinamide
Activity against TB	**Bactericidal** for semi-dormant *M. tuberculosis*. Mechanism unclear.
Cross-resistance	None reported.
Dose	**Adults:** 25-40 mg/kg/day **Children:** [WHO 2022, AAP 2021, ATS/CDC/ERS/IDSA 2019] 30–40 mg/kg/dose. **Renal failure:** 25 mg/kg/dose 3 times per week (not daily). Dose after hemodialysis. **Obesity:** Serum concentrations should be monitored, as dosing with lean body weight likely will lead to under-dosing
Route of administration	Oral; not available parenterally.
Preparation	500 mg scored or unscored tablet.
Storage	Store the tablets at room temperature.
Pharmacokinetics	**Peak concentration** is 1–4 hours after an oral dose. **Peak concentrations** of 20–40 mcg/mL are expected after a daily dose. When giving 50 mg/kg intermittently, 60-80 mcg/mL can be expected. **Blood sampling times** 2 and 6 hours post dose. **Half-life** (adult, normal renal function) 6-10 hours.
Oral absorption	Well absorbed from the GI tract.
CSF penetration	Concentrations equivalent to serum.
Special circumstances	**Use in pregnancy/breastfeeding:** In the U.S. PZA was historically avoided in the TB regimens of most pregnant women with drug-susceptible TB due to lack of controlled data during pregnancy. However, WHO and the International Union Against TB and Lung Disease recommend routine use of PZA during pregnancy (as do some jurisdictions in the U.S.), and toxicity to the fetus has not been documented. Can be used for drug-resistant TB when the isolate is susceptible to PZA. Can be used while breastfeeding. **Use in renal disease:** Metabolites are cleared by the kidneys; dose 3 times a week and after hemodialysis. **Use in hepatic disease:** Use with caution; PZA is associated with hepatotoxicity in about 1% of patients. It can be quite severe and worsen even after stopping treatment.
Adverse reactions	• Gout (hyperuricemia) and arthralgias • Hepatotoxicity • Rash • Photosensitivity • Gastrointestinal upset

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PYRAZINAMIDE (PZA, Z) [2 of 2]

Contraindications	**Allergy to pyrazinamide; severe gout.**
Monitoring	Monitor transaminases; uric acid can be monitored in patients with history of gout or who receive medications that alter uric acid excretion. An elevated uric acid is an expected finding in every patient on pyrazinamide. If not present, may indicate patient is not taking the drug or there is malabsorption.
2022 wholesale cost 30-day supply, 60-kg person	$146 (outpatient public health pricing, 340B)
Patient instructions	May be taken with or without food. This medicine may cause a rash after sun exposure; limit your sun exposure. **Call your doctor right away if you have any of these side effects:** • Rash or itching • Pain or swelling in the joints • Nausea, vomiting, abdominal pain, or reduced appetite • Light-colored bowel movements, dark-colored urine, yellowing of your skin or the white of your eyes

RIFABUTIN (RFB) [1 of 2]

Drug class	Rifamycin
Trade name	Mycobutin
Activity against TB	**Bactericidal;** same mechanism of activity as rifampin (inhibits RNA polymerase).
Cross-resistance	Cross-resistance among the rifamycin class of drugs is typical. In <20% of strains that are resistant to rifampin, rifabutin may retain susceptibility *in vitro*. The clinical significance of this is unknown.
Dose	**Adults:** 5 mg/kg/dose (usual dose 300 mg, though doses up to 600 mg are sometimes used). Dose adjustments sometimes required when dosing with interacting drugs. **Children:** The pediatric dose is not established, but doses of 5–10 mg/kg/day have been used (higher doses have been recommended for children < 1 year of age). Caution should be used in very young children in whom visual changes might not be obvious. **Renal failure:** No dose adjustment in mild renal insufficiency. For creatinine clearance less than 30 mL/minute, the usual dose may be used, but monitor drug concentrations to avoid toxicity. **Concomitant medications:** Dosage adjustment may be required, particularly with anti-retroviral therapy use. See https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/whats-new If given with ritonavir or cobicistat, begin with 150 mg daily. If given with efavirenz, begin with 600 mg daily.
Route of administration	Oral; not available parenterally.
Preparation	150 mg capsule.
Storage	Capsules should be kept at room temperature.
Pharmacokinetics	**Peak concentration** is reached 3–4 hours after a dose. **Peak concentration** should be between 0.45 and 0.9 mcg/mL. Dose adjustments should be considered for patients with concentrations < 0.3 or > 1.0 mcg/mL (low concentrations predict risk of emergence of drug resistance). Rifabutin concentrates in tissues: in lung tissues, concentrations may reach 10–20 times that in serum. **Blood sampling times** 3 and 7 hours post dose. May give 1 hour before companion drugs to limit to 2 blood draws. **Half-life** (adult, normal renal function): **biphasic:** about 3-4 hours initially, then >30 hours at lower concentrations.
Oral absorption	Well absorbed from the GI tract.
CSF penetration	Little published data on CSF penetration; available evidence suggests moderate penetration into CSF.

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RIFABUTIN (RFB) [2 of 2]

Special circumstances	**Use in pregnancy/breastfeeding:** Insufficient data in pregnancy. Unknown effects from breastfeeding. **Use in renal disease:** Used without dose adjustment in mild renal insufficiency. For creatinine clearance less than 30 mL/minute, the usual dose may be used, but monitor drug concentrations to avoid toxicity. **Use in hepatic disease:** Use with caution and additional monitoring in liver disease. Dose adjustments necessary for drug interactions—especially HIV drugs. See https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection/whats-new-guidelines
Adverse reactions	• Leukopenia (dose dependent); thrombocytopenia. • Rashes and skin discoloration (bronzing or pseudojaundice). • Anterior uveitis. • Hepatotoxicity similar to that of rifampin. • Drug interactions with many other drugs—but only 40% of that seen with rifampin. • Rifabutin concentrations may be affected by other drugs. • Arthralgias.
Contraindications	**Rifamycin hypersensitivity.** Data are lacking on cross-sensitivity to rifabutin in patients with hypersensitivity. Use with caution, with careful monitoring of patient for development of hypersensitivity. Should not be used for patients with MDR-TB unless susceptibility to rifabutin documented.
Monitoring	Increased liver function monitoring; monitor drug concentrations of interacting medications; blood counts and vision screening.
2022 wholesale cost 30-day supply, 60-kg person	$195 (outpatient public health pricing, 340B)
Patient instructions	May be taken with or without food; if it bothers your stomach, try taking it with food. It is normal for your urine, tears, and other secretions to turn a brownish-orange color when taking this medicine. Sometimes skin becomes discolored. Soft contact lenses may become discolored while you are on this medicine. Make sure your doctor knows all the medicines you take, as there are many drugs that interfere with this one. Avoid the use of oral hormone-based birth control methods because rifabutin may decrease their effectiveness. **Call your doctor right away if you have any of these side effects:** • Any eye pain, change in vision, or sensitivity to light • Fever, chills, or sore throat • Pain or swelling in the joints • Yellowing of the skin or eyes or dark urine • Nausea or vomiting • Unusual tiredness or loss of appetite

RIFAMPIN (RIF, R) [1 of 2]

Drug class	Rifamycin
Trade name	Rifadin (also known as rifampicin)
Activity against TB	**Bactericidal;** inhibits protein synthesis; cross-resistance with other rifamycins.
Cross-resistance	Cross-resistance among the rifamycin class of drugs is typical. In <20% of strains resistant to rifampin, rifabutin may retain susceptibility *in vitro*. The clinical significance of this is unknown.
Dose	**Adults:** 10 mg/kg/day (PO or IV). Usual dose 600 mg daily; doses up to 40 mg/kg being studied. **Children:** [AAP 2021] 15-20 mg/kg/day (max 600 mg/day) 20-30 mg/kg/day for infants and toddlers and for some children with CNS or disseminated disease. **Renal failure:** No adjustment required. **Concomitant medications:** Rifampin interacts with multiple drug classes via CYP 3A4 or 2C9 induction. Rifampin decreases effect of drugs including certain integrase strand inhibitors, protease inhibitors, opioids, oral contraceptives, warfarin and other anticoagulants. Use of drug interaction tools is recommended for new rifampin starts.
Route of administration	Oral or intravenous.
Preparation	150 and 300 mg capsules; lyophilized powder for injection: 600 mg/vial; contents of capsules can be mixed with liquid or semi-soft vehicles. Extemporaneously prepared oral solutions have unproven homogeneity and shelf life. Immediate administration of the dose after mixing capsular contents in a vehicle is ideal.
Storage	Capsules and powder should be kept at room temperature; powder suspended in saline is stable for 24 hours; powder suspended in dextrose solutions is stable for 4 hours.
Pharmacokinetics	**Peak time to concentration** after an oral dose is 1–4 hours. **Peak concentrations** of 8 to 24 mcg/mL are expected. Dose increase should be strongly considered for low concentrations (but not for delayed absorption), as rifampin exhibits a dose response in treatment of TB. **Blood sampling times** 2 and 6 hours post dose. **Half-life** (adult, normal renal function): about 3-4 hours initially, and about 2 hours after 2 weeks due to auto-induction of clearance.
Oral absorption	Usually rapid absorption, may be delayed or decreased by high-fat meals.
CSF penetration	Rifampin CSF penetration is variable and typically achieves only 10–20% of serum concentrations in CSF (may be better in the face of inflamed meninges), but this may still be an important contribution to the regimen. Some authors recommend increased doses of rifampin in patients with TB meningitis.

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RIFAMPIN (RIF, R) [2 of 2]

Special circumstances	**Use in pregnancy/breastfeeding:** Recommended for use in pregnancy; can be used while breastfeeding. **Use in renal disease:** Can be used without dose adjustment. **Use in hepatic disease:** Use with caution, can be associated with hepatotoxicity.
Adverse reactions	**Many drug interactions.** • Orange staining of body fluids. • Rash and pruritus. • GI upset, flu-like syndrome (usually only with intermittent administration). • Hepatotoxicity. • Hematologic abnormalities (thrombocytopenia, hemolytic anemia).
Contraindications	**Rifamycin allergy;** due to **drug interactions,** may be contraindicated with concurrent use of certain drugs.
Monitoring	Liver function monitoring if appropriate (if given with other hepatotoxic medications or if there are symptoms of hepatotoxicity); monitor drug concentrations of interacting medications.
2022 wholesale cost 30-day supply, 60-kg person	$16 (outpatient public health pricing, 340B)
Patient instructions	Best taken without food; if it bothers your stomach, try taking it with a small amount of food. It is normal for your urine, tears, and other secretions to turn an orange color when taking this medicine. Soft contact lenses may become discolored while you are on this medicine. Make sure your doctor knows all the medicines you take because many drugs can interfere with this one. Avoid the use of oral hormone-based birth control methods because rifampin may decrease their effectiveness. **Call your doctor right away if you have any of these side effects:** • Rash • Fevers or flu-like illness • Nausea, vomiting, abdominal pain, or reduced appetite • Light-colored bowel movements, dark-colored urine, yellowing of your skin or the white of your eyes

RIFAPENTINE (RPT) [1 of 2]

Drug class	Rifamycin
Trade name	Priftin
Activity against TB	**Bactericidal;** same mechanism of action as rifampin, inhibits RNA polymerase. 100% cross-resistant with rifampin.
Cross-resistance	Cross-resistance among the rifamycin class of drugs is typical. In <20% of strains resistant to rifampin, rifabutin may retain susceptibility *in vitro*. The clinical significance of this is unknown.
Dose for active tuberculosis disease	**Adults:** 1200 mg daily.* Best given with food. **Children:** Participants in Study 31 trial supporting use of 4 month drug-susceptible TB regimen were >12 and older and received RPT 1200 mg daily. Pill burden may be a limitation for young children. *1200 mg weekly if using RIFAQUIN regimen (See **Chapter 4, *Treatment*** for details)
Dose for LTBI	**Adults:** 900 mg once weekly for 12 doses given with INH 900 mg. **Children:** (12 and older), once weekly dose for 12 weeks based on weight (10.0-14.0 kg = 300 mg; 14.1-25.0 kg = 450 mg; 25.1-32.0 kg = 600 mg; 32.1-49.9 kg = 750 mg). 3HP regimen not approved for children <2 years **Renal failure:** No adjustment required. Only 17% of ingested dose is excreted renally. **Concomitant medications:** Dosage adjustment may be required for concurrent medications. Concurrent treatment with most anti-retroviral drugs is not recommended, as anti-retroviral drug concentrations are substantially reduced, as they are with rifampin. On the other hand, rifapentine plasma concentrations are not affected by most other drugs, based on current data.
Route of administration	Oral
Preparation	150 mg tablets
Storage	Tablets should be stored at room temperature
Pharmacokinetics	**Time to peak concentration** after an oral dose is 5– 6 hours. **Peak concentrations** after a 600 mg dose are expected to be 8 – 30 mcg/mL; higher with 900 to 1200 mg doses. The half-life is approximately 13 hours. **Blood sampling times** Trough and 5-6 hours post dose. **Half-life** (adult, normal renal function): about 15-18 hours
Oral absorption	Oral bioavailability is 70%. Peak concentration and AUC are increased if given with a meal.
CSF penetration	No information available.

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RIFAPENTINE (RPT) [2 of 2]

Special circumstances	**Use in pregnancy:** Pregnancy category C. Use only if potential benefit outweighs possible risk. **Use in renal disease:** Insufficient data, but likely to be safe since only minimally excreted by the kidneys. **Use in hepatic disease:** Pharmacokinetics are very similar to normal volunteers in persons with mild to severe liver impairment. **Dose adjustments:** Not necessary to adjust rifapentine dosage due to drug interactions, but may be needed for concurrent drugs, as is the case for rifampin.
Adverse reactions	**Many drug interactions.** • Red-orange staining of body fluids • Rash and pruritis • Hypersensitivity reaction • Hepatoxicity • Hematologic abnormalities
Contraindications	History of hypersensitivity to any of the rifamycins (i.e., rifampin or rifabutin)
Monitoring	Liver function monitoring if appropriate (if given with other hepatotoxic medications or if there are symptoms of hepatotoxicity); monitor drug concentrations of interacting medications.
2022 wholesale cost 30-day supply, 60-kg person	$76 (outpatient public health pricing, 340B)
Patient instructions	Rifapentine may produce a reddish coloration of your urine, sweat, sputum, tears, and breast milk — be aware that your contact lenses or dentures may be permanently stained. The reliability of oral or other systemic hormonal contraceptives may be affected; consider using alternative contraceptive measures. If you are prone to nausea, vomiting, or gastrointestinal upset, taking rifapentine with food may be useful. **Call your doctor right away if you have any of these side effects:** • Rash or itching • Fevers or flu-like illness • Nausea, vomiting, abdominal pain, or reduced appetite

STREPTOMYCIN (SM, S) [1 of 2]

Drug class	Aminoglycoside
Trade name	Streptomycin sulfate
Activity against TB	**Bactericidal;** inhibits protein synthesis.
Cross-resistance	Rarely may be cross-resistant to kanamycin.
Dose (all once daily)	**Adults:** 15 mg/kg/day in a single daily dose, 5–7 days per week. Some experts suggest 15 mg/kg/dose, 2–3x/week can be used after culture conversion is documented after initial period of daily administration (some experts use up to 25 mg/kg/dose for intermittent therapy; monitor concentrations). **> 59 years of age:** Many experienced clinicians prefer to use a lower starting dose of 10 mg/kg/dose (max 750 mg) 5-7x/week or 2-3x/week after initial period and consider follow-up with drug concentrations. **Children:** [ATS/CDC/ERS/IDSA 2019] 20-40 mg/kg/day (max 1000 mg/day); 5-7 days per week **Renal failure:** 12–15 mg/kg/dose after hemodialysis 2-3x/week (not daily). **Markedly obese individuals** should have an adjusted dose due to the decreased distribution of extracellular fluids in adipose tissues. Dosing based on actual weight will give supratherapeutic concentrations. **For dosing, use adjusted weight as follows:** Ideal body weight + 40% of excess weight Ideal body weight (men): 50 kg plus 2.3 kg/inch over 5 ft Ideal body weight (women): 45 kg plus 2.3 kg/inch over 5 ft Concentrations should be followed closely.
Route of administration	Intravenous or intramuscular (has been used intrathecally and intraperitoneally). Not absorbed orally.
Preparation	1000 mg vial for injection.
Storage	Store in the refrigerator.
Pharmacokinetics	For intravenous administration, infuse over 30-60 minutes for adults; 1–2 hours for children; intramuscular absorption is complete within 4 hours and peak concentrations are achieved at 1–2 hours. For intravenous administration, infuse over 30-60 minutes for adults; 1–2 hours for children; intramuscular absorption is complete within 4 hours and peak concentrations are achieved at 1–2 hours. Intramuscular absorption might be delayed if the same site is used consistently. Obtaining a drug concentration 2 and 6 hours post dose provides complete information for calculating C_{max}, C_{min}, and half-life. Nonogram dosing and random sampling late in the dosing interval are discouraged. **Peak concentrations** for a 15 mg/kg dose are between 35 - 45 mcg/mL. **Peak concentrations** for a 25 mg/kg dose are between 65 - 80 mcg/mL. **Trough concentrations** are generally < 5 mcg/mL in patients with normal renal function. **Blood sampling times:** 2 and 6 hours post dose. **Half-life:** 2-3 hours with normal renal function.
Oral absorption	There is no significant oral absorption.

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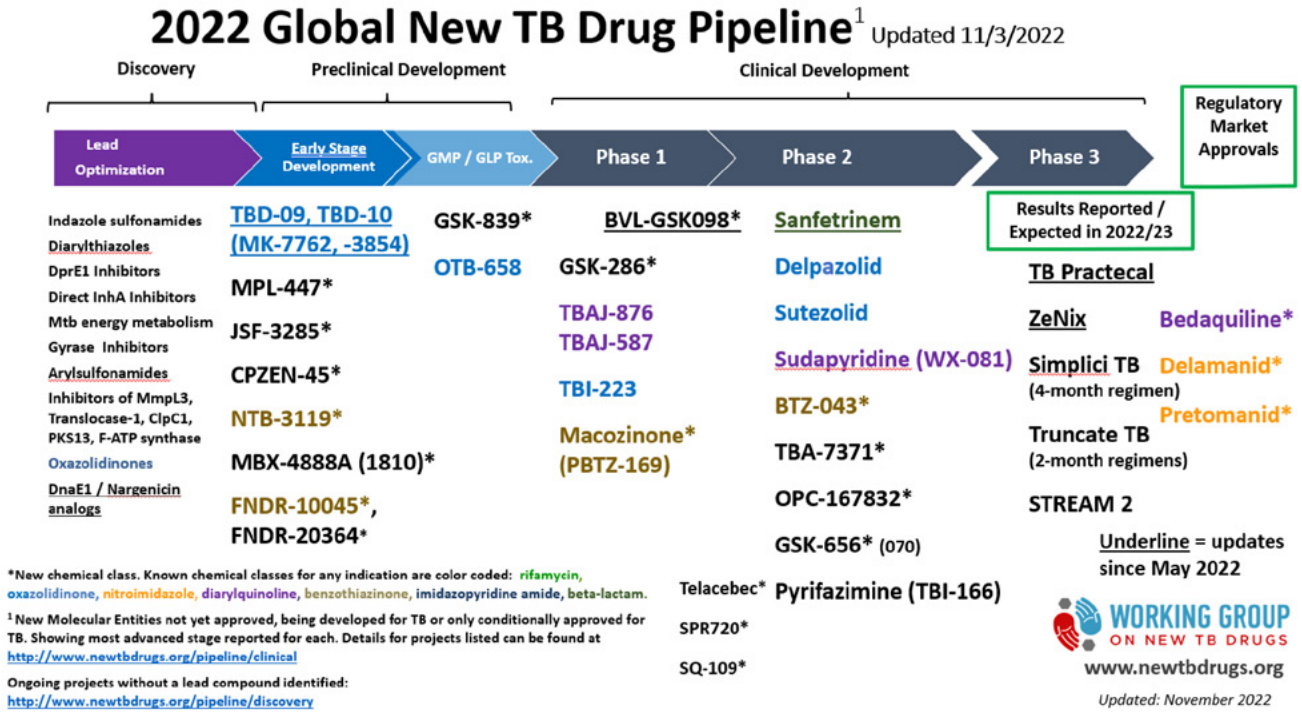
STREPTOMYCIN (SM, S) [2 of 2]

CSF penetration	Variable penetration; appears to penetrate inflamed meninges better.
Special circumstances	**Use in pregnancy/breastfeeding:** Avoided in pregnancy due to documented cases of congenital deafness. Can be used while breastfeeding. **Use in renal disease:** Use with caution. Concentrations should be monitored for patients with impaired renal function. Interval adjustment is recommended for renal impairment or hemodialysis. See "Dose – Renal Failure" (previous page). The drug is variably cleared by hemodialysis; see **Chapter 7, *Co-morbidities and Special Situations – Renal Failure.*** **Use in hepatic disease:** Drug concentrations not affected by hepatic disease (expect a larger volume of distribution for alcoholic cirrhotic patients with ascites). Presumed to be safe in severe liver disease; however, use with caution—some patients with severe liver disease may progress rapidly to hepato-renal syndrome. **Diuretic use:** Coadministration of loop diuretics and aminoglycoside antibiotics carries an increased risk of ototoxicity.
Adverse reactions	• Nephrotoxicity: monitor BUN and serum creatinine. • Ototoxicity (hearing loss): Increased with advanced age and prolonged use. • Vestibular toxicity. • Local pain with IM injections. • Electrolyte abnormalities, including hypokalemia, hypocalcemia, and hypomagnesemia.
Contraindications	**Pregnancy** (congenital deafness seen with streptomycin and kanamycin use in pregnancy); **hypersensitivity to aminoglycosides;** caution with renal, vestibular, or auditory impairment.
Monitoring	Monitor renal function by documenting creatinine at least monthly (more frequently if renal or hepatic impairment); document creatinine clearance if there is baseline renal impairment or any concerns; document baseline and monthly audiology exam. Question patient regularly about vestibular complaints and perform serial vestibular exams. Document peak and trough concentrations at baseline if there is any question about renal function. Some experts monitor aminoglycoside concentrations routinely, regardless of renal function. Monitor concentrations serially for patients with impaired renal function.
2022 wholesale cost 30-day supply, 60-kg person	$183 (outpatient public health pricing, 340B)
Patient instructions	Store streptomycin in the refrigerator. **Call your doctor right away if you have:** • Changes in your hearing, or ringing or fullness in your ears • Feeling dizzy, weak, or unsteady • Trouble breathing • Swelling of feet or ankles • Decreased urination • Swelling, pain, or redness at your IV site • Muscle twitching or weakness

New Anti-TB Drugs in the Pipeline



Downloaded December 6, 2022.

For updated information, see https://www.newtbdrugs.org/pipeline/clinical

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