Pyrazinamide (Z)	Streptomycin (S)	Ethambutol (E)	Isoniazid (INH / H)	Rifampicin (R)	Feature
Tuberculocidal	Bactericidal	Tuberculostatic	Bactericidal for rapidly growing bacilli, static for non-growing	Bactericidal	**Type / Nature**
Inhibits mycolic acid synthesis	Inhibits protein synthesis by binding to 30S ribosomal subunit	Inhibits mycolic acid synthesis	Inhibits mycobacterial catalase–peroxidase and mycolic acid synthesis	Inhibits bacterial RNA synthesis by binding to mycobacterial DNA-dependent RNA polymerase → blocks polymerizing function	**Mechanism of Action**
Intracellular bacilli	Extracellular bacilli	Extra- & intracellular	Extra- & intracellular bacilli	Extra- & intracellular bacteria	**Main Target Site**
Active on *M. tuberculosis*, especially intracellular residual forms	Active on extracellular *Mycobacterium tuberculosis*	Active on *Mycobacterium tuberculosis*	Specific for *Mycobacterium tuberculosis*	Broad spectrum antibacterial (G+ & G–): *Staph, Strept, N. meningitides, H. influenzae, Legionella, Clostridium difficile*; Anti-mycobacterial (TB, leprosy); Antiviral (poxvirus)	**Spectrum / Activity**
Well distributed; oral (not specified otherwise)	IM injection (systemic use)	Oral	Completely absorbed orally; inhibited by aluminum-containing antacids	Well absorbed orally; food interferes (take on empty stomach)	**Absorption**
Distributed in all body fluids	Mainly extracellular	Acts both extra- & intracellular	Penetrates all body tissues, tubercular cavities, placenta, meninges	Widely distributed: body fluids, intracellular, tubercular cavities, caseous masses, placenta	**Distribution**
Not specified	Not specified	Not specified	In liver by acetylation (INH acetyltransferase); side effects more common in slow acetylators	In liver → active de-acetylated metabolite; potent inducer of CYP450 → many drug interactions; auto-induction of its metabolism (↑ clearance after 2 weeks)	**Metabolism**
Not specified	Not specified	Renal (contraindicated if CrCl < 50 ml/min)	Excreted in urine → reduce dose in renal impairment	Mainly in bile; some in urine; 30–70% undergo enterohepatic circulation	**Excretion**
—	—	—	—	Metabolites orange-red → red urine, sweat, staining of clothes	**Color / Physical Effect**
Hepatotoxicity (dose-dependent), hyperuricemia (inhibits urate excretion)	Ototoxicity, nephrotoxicity, neuromuscular block	Optic neuritis (loss of visual acuity & color vision, reversible), hyperuricemia (worsens gout)	Peripheral neuropathy (due to pyridoxine deficiency), hepatotoxicity, CNS toxicity (seizures, optic neuritis, memory loss, stupor), hemolysis (G6PD deficiency), SLE-like syndrome	Hepatitis (major), interstitial nephritis, acute tubular necrosis, hemolytic anemia, flu-like symptoms, enzyme inducer (drug interactions)	**Main Adverse Effects**
Used mainly during first 2 months for sterilizing activity	Limit to ≤2 g/day; used in severe or life-threatening TB	Stop at first sign of visual impairment; toxicity reversible	Pyridoxine (Vit. B6) 10 mg/day prophylaxis; 100 mg/day for treatment of neuropathy	Avoid drug interactions (warfarin, corticosteroids, OCPs, digoxin); enzyme inducer	**Prevention of Toxicity / Notes**
—	—	Children <6 years, renal impairment (CrCl <50 ml/min), hyperuricemia	—	—	**Contraindications**
Effective early; good sterilizing activity by killing residual intracellular bacilli	Only *antibiotic* among 1st line; for severe disseminated forms (e.g. meningitis)	Added to TB regimen to prevent resistance and hasten sputum conversion	Cheapest & keystone of TB therapy	Broad spectrum; used in TB, leprosy, meningitis, osteomyelitis, endocarditis; prophylaxis	**Special Importance**
—	—	—	None mentioned, but metabolism depends on acetylator status	Potent enzyme inducer → increases metabolism of many drugs (warfarin, corticosteroids, contraceptive pills, digoxin); self-induction	**Enzyme Induction / Interactions**

2nd line drugs

Para-aminosalicylic acid (PAS)	Rifapentine	Rifabutin	Cycloserine	Quinolones (Ciprofloxacin, Ofloxacin, Sparfloxacin)	Aminoglycosides (Amikacin, Kanamycin)	Feature
Used to delay development of resistance; not used nowadays	Used in resistant cases; similar to rifampicin	Used in resistant cases; similar to rifampicin	Used in resistant cases; broad spectrum antibiotic	Used in resistant cases combined with ≥2 anti-TB drugs	Used when resistance to 1st line drugs, failure of clinical response, or contraindication to 1st line	**Indications**
Tuberculostatic; active only on *M. tuberculosis*	Similar to rifampicin in spectrum, action and toxicity	Similar to rifampicin in spectrum and action	Broad spectrum (static); reaches CSF well	Bactericidal; affect resistant *M. tuberculosis*	Bactericidal; affect both typical and atypical mycobacteria	**Effect on Mycobacteria**
Competitively inhibits dihydrofolate reductase (structural analogue of PABA) → inhibits folic acid synthesis	Inhibits bacterial RNA synthesis (like rifampicin)	Inhibits bacterial RNA synthesis (like rifampicin)	Competitively inhibits enzyme (as analog of PABA) → inhibition of folic acid synthesis via dihydrofolate reductase	Not detailed in text	Not detailed in text	**Mechanism of Action**
Selective for mycobacterial dihydrofolate reductase	Anti-mycobacterial	Anti-mycobacterial (TB, leprosy)	Broad spectrum	Broad spectrum against mycobacteria	Typical & atypical *Mycobacterium*	**Spectrum**
Not mentioned	Slower and prolonged action; similar absorption/ excretion to rifampicin	Absorbed orally; excreted in bile & urine (orange-yellow metabolites)	Reaches CSF well	Not mentioned	Not mentioned	**Pharmacokinetics (PKs)**
Not mentioned	Enzyme inducer; contraindicated in HIV patients (destroys antiviral drugs)	Cross tolerance with rifampicin; less enzyme inducer → fewer drug interactions	Not mentioned	Not mentioned	Not mentioned	**Cross Tolerance / Enzyme Induction**
High doses needed; significant side effects (not specified)	Similar toxicity to rifampicin	Less enzyme induction → fewer drug interactions	CNS side effects	Not mentioned (relatively high toxicity as 2nd line)	Not mentioned (but relatively high toxicity as 2nd line)	**Adverse Effects**
Least active drug; tuberculostatic; delays resistance; not used nowadays due to side effects	Contraindicated in HIV patients due to enzyme induction	Orange-yellow metabolites in excretion	Causes CNS side effects; broad spectrum	Always combined with ≥2 anti-TB drugs	Bactericidal, used for resistant or atypical TB	**Special Points / Notes**
				Relatively high	Relatively high	**Overall Toxicity Level**
High (limits use)	Similar toxicity to rifampicin	Less toxic than rifampicin	Relatively high (CNS toxicity)