# Drug Treatment of Tuberculosis

| Drug | MOA | Uses | Side Effects | Notes |
|---|---|---|---|---|
| **First Line Drugs (Primary)** | | | | |
| **Isoniazid (INH)** | - A **prodrug** activated by a mycobacterial catalase–peroxidase (KatG)<br>-The activated Isoniazid **blocks mycolic acid synthesis**, and consequently mycobacterial cell wall synthesis, leading to a **bactericidal** effect | -Treatment of TB | -**Hepatitis**: in about 1%<br>-Anorexia, nausea, vomiting, jaundice, pain, and death (depend on age, alcohol use, pregnancy)<br>-**Neuropathy**: 10-20% (due to **pyridoxine (Vit B6) deficiency**): occurs more in slow acetylators, malnutrition, alcoholism, DM, AIDS, and uremia<br>-**Neurotoxicity**: memory loss, psychosis, and seizures<br>-Hematologic, tinnitus, GIT, and drug interactions | - Most active, it is a small molecule and water soluble<br>- Structurally related to Pyridoxine (Vit B6)<br>- Readily absorbed and widely distributed so it penetrates into macrophage easily<br>-Metabolized by acetylation: there are slow and fast acetylators |
| **Rifampin** | -Binds to the beta subunit of bacterial **RNA polymerase** and therefore inhibits RNA synthesis → prevent the synthesis of bacterial proteins<br>-**Bactericidal** (dose defendant) | -TB<br>-Leprosy<br>-Meningococcal Carrier State<br>-**Prophylaxis** in H.influenzae<br>-Serious Staph Osteomyelitis<br>-**Drug of choice** for valve endocarditis<br>-Streptomyces mediterranei<br>-Enterococci and chlamydia | ✷**Toxicity**:<br>- **Mild**: Imparts harmless orange color to secretions (tears, urine, sweat), rashes and flu-like syndrome<br>-**Serious**: Can cause hepatitis and is a liver enzyme inducer (stimulates liver enzyme activity → decrease in the serum levels of many drugs) | - Well absorbed, highly bound to proteins, and widely distributed<br>-Metabolized in the liver and exhibits enterohepatic recirculation<br>-If only a small dose is given or the period of treatment is short, the effect becomes bacteriostatic<br>-In Jordan, use restricted for TB |
| **Streptomycin** | -Binds irreversibly to **small subunit of rRNA** | -Used for plague, Tularemia, Brucellosis, and endocarditis | ✷**Toxicity:**<br>-Allergy, fever, rashes, and pain after IM injection<br>-**Vestibular toxicity (Irreversible)**<br>-Nephrotoxicity | -A second-line anti-tuberculous agent but it could be used as a first line agent |
| **Second Line Drugs** | | | | |
| **Ethionamide** | -Related to Isoniazid: it blocks mycolic acid synthesis | | -**Poorly tolerated**: severe GIT irritation, neurotoxic and hepatotoxic | -Given orally and has a good distribution |
| **Capreomycin** | -Peptide protein synthesis inhibitor | | Nephrotoxic, ototoxic, local pain (at injection site) and sterile abscesses | -Injectable |
| **Cycloserine** | -Inhibits cell wall synthesis (bactericidal) | | -Peripheral **neuropathy and CNS toxicity:** depression and psychosis | -We give it to the patient in the hospital to ensure supervision |
| **Amikacin** | | -Used with **Atypical mycobacteria and multidrug-resistant strains** | | |

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| **Para-Amino-Salicylic Acid (PAS)** | -Folate synthesis antagonist | | -GI toxicity, hypersensitivity reactions, and crystalluria | -Well absorbed, dose 8-12 gm/day<br>-Widely distributed, except in CNS<br>-Excreted in Urine |
| **Fluoroquinolone** | | -Important addition to the treatment regimen | | **Resistance develops rapidly if used alone |
| **Linezolid** | | - Used for multidrug-resistant strains<br>- **Drug of last resort** | -Bone marrow suppression, irreversible peripheral and optic neuropathy | |
| **Rifabutin & Rifapentine** | -Related to Rifampin: inhibit bacterial RNA polymerase | -Rifabutin is indicated in place of Rifampin in the **treatment of TB in HIV-infected patients** receiving protease inhibitors or nonnucleoside reverse transcriptase inhibitors (E.G **efavirenz** which are metabolized by CYP450) | -Like rifampin: inducers for CYP P450 enzymes (Rifabutin is a less potent inducer) | |
| **Treatment of Atypical Mycobacteria** | | | | |
| **Erythromycin, Sulfonamides and Tetracycline** | | - M. tuberculosis complex | | |
| **Azithromycin or Clarithromycin, + Ethambutol + Ciprofloxacin** | | -M. avium complex (Important and common cause of disseminated TB in late stages of AIDS) | | |

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