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| **CELL WALL SYNTHESIS INHIBITIORS** | | | | | | |
| **DRUG** | **SAR** | **Type of inhibitor** | **Mechanism of Action (MOA) & Target** | **Mechanism of Resistance (MOR)** | **Spectrum** | **TOXICITIES** |
| **Fosfomycin** | * PEP mimic * Reactive epoxide group | Irreversible inhibitor/ Suicide inhibitor | MOA: Inhibits PEP transferase irreversibly which  inhibits cell peptidoglycan synthesis - specifically NAM synthesis  (Stage 1: Synthesis of Building Blocks)  Bactericidal  Target: UDP-NAG phosphoenoylpyruvuyl (PEP) transferase = MurA | 1) Mutation of active site (Microbe has Cysteine instead of Asp)  2) Mutation of glycerophosphate transporter | Broad – both Gram positive and Gram negative | Low  Nausea, vomiting, diarrhea, hypersensitivity, skin rash |
| **Cycloserine** | * D-Ala analogue * 5-membered ring | Non-covalent/ competitive inhibitor – substrate mimic  Binds 100x more tightly to the enzymes (rigid structure) | MOA; Competitive inhibitor of Alanine racemase and transferase  Which inhibits cell peptidoglycan synthesis.  (Stage 1: Synthesis of Building Blocks)  Bactericidal  Target: D-Ala-D-Ala racemase and D-Ala-D-Ala ligase | Overexpression of D-alanine racemase (AlrA) | Broad – both Gram positive and Gram negative | Neurotoxic  CNS disturbance, anxiety, confusion and drowsiness |
| **Bacitracin** | - Large molecule with many peptide bonds |  | MOA: Binds to pyrophosphatase in the presence of Magnesium,thus preventing regeneration of  Bactoprene. It is more active if zinc is already present in the preparation, aiding in the binding to pyrophosphatase  Which inhibits cell peptidoglycan synthesis.  (Stage 2: Synthesis of Membrane-bound Precursors and Polymerization)  Bactericidal  Target: Pyrophosphatases | Failure to penetrate membrane | Gram positive only – too big to get through outer membrane of Gram negative | Nephrotoxicity – not used systemically\*/topical |
| **Vancomycin** | Screen Shot 2016-11-17 at 3.39.09 PM.png   * Large molecule with many peptide bonds * Circled atoms form hydrogen bonds with D-Ala-D-Ala | Competitive/ reversible | (Stage 2: Synthesis of Membrane-bound Precursors and Polymerization)  Binds directly to the D-Ala-D-Ala terminal to prevent peptide cross-linking  Bactericidal  Target: D-Ala-D-Ala | 1. Alter the substrate – make D-Ala-D-Lac. Results in loss of H-bond between vancomycin and dipeptide. 2. Thicker cell wall of bacterium | Gram positive only | Redman syndrome (if infused too quickly), Nephrotoxicity, Hearing loss, Rash |