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| **DNA Topoisomerase inhibitors** | | | | | |
| **Drug Class**  **(Examples)** | **SAR** | **Mechanism of Action (MOA) & Target** | **Mechanism of Resistance (MOR)** | **Indication/Spectrum** | **Toxicities/DDI’s** |
| Fluoroquinolones  (Ciprofloxacin, Levofloxacin, Moxifloxacin) | **Position 1:** nitrogen can allow substitutions of alkyl (Me, Et, cPr) or aryl (2,4-difluorophenyl) groups  **Position 2:** can be either a carbon or nitrogen  **Position 3:** must be unsubstituted carboxylic acid  **Position 4:** must be ketone  **Position 6:** fluorine substitution increases activity and broadens spectrum  **Position 7:** substitution with nitrogen containing heterocycles (piperazine ring) broadens spectrum; potential for zwitterion  **Position 8:** substitution with small polar groups (OCH3, F, Cl) increases activity | MOA: Irreversibly inhibits topoisomerase (DNA gyrase) enzymes, which inhibits relaxation of supercoiled DNA and promotes breakage of double stranded DNA.  Bactericidal  Target: Topoisomerase II (DNA Gyrase) | 1. Mutation to the quinolone-resistance determining region (QRDR) of gyrase that affects the binding of fluoroquinolones  2. Active drug efflux  3. Decrease drug uptake (reduced permeability) | Broad spectrum (increases with increasing generation) | Tendon rupture, QT prolongation, Phototoxicity. Rashes, Peripheral neuropathy  DDI: Chelation with cations, synergistic inhibition of GABA receptor with NSAIDs |