

Antifolate Antibiotics

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Sketchy bot link : https://t.me/Selda_Sketchy_Bot

اللهم إنا نستودعك أهلنا في غرة أحيمهم يا الله بعينك
التي لا تنام

Drug	Mechanism of action	Spectrum	Adverse effects
<u>Sulfonamides</u> <u>1. Oral, absorbable :</u> sulfamethoxazole and sulfadiazine <u>2. Oral, non-absorbable:</u> Sulfasalazine <u>3. Topical :</u> sulfacetamide & silver sulfadiazine	Inhibit dihydropteroate synthase , preventing PABA from forming folic acid Mechanism of resistance : - - Some bacteria lack dihydropteroate synthase and are not susceptible to sulfonamides. - overproduction of PABA - enzyme with low affinity to sulfonamides - Impair cell permeability	<i>Board spectrum</i> : gram +ve , gram -ve , Nocardia , chlamydia trachomatis , E.coli , klebsiella , salmonella , shigella , Enterobacter , Pneumocystis jiroveci, Toxoplasma Poor against anaerobes	1. Exfoliative dermatitis 2. Stevens- Johnson syndrome 3. Crystalluria 4. G6PD deficiency hemolysis 5. Aplastic anemia , granulocytopenia , thrombocytopenia 6. Mucous membrane eruptions can occur without dermatitis. 7. Contraindicated in pregnancy (teratogenic)
<u>Trimethoprim</u> Excreted in urine partially as metabolites , dose should be reduced in renal failure Concentrates in vaginal and prostatic fluids	Inhibits bacterial dihydrofolate reductase , blocking the conversion of dihydrofolic acid to tetrahydrofolic acid Mechanisms of resistance : - reduced cell permeability - Overproduction of dihydrofolate reductase - Altered dihydrofolate = low binding to drug ★	E.coli (UTIs) either alone or in combination with sulfamethoxazole Salmonella Shigella Pneumocystis jiroveci- IV infusion	Megaloblastic anemia Leukopenia Granulocytopenia Diarrhea Hyperkalemia and hyponatremia
<u>Co-trimoxazole</u>	Combination of trimethoprim & sulfonamide	—	—
Pyrimethamine	Inhibits Protozoal dihydrofolate reductase	Protozoa	-

Fluoroquinolones

Inhibits DNA gyrase (topoisomerase II) & Topoisomerase IV

Active against : Gram - ve (pseudomonas , Neisseria , Haemophilus) , Moderate gram +ve (streptococcus pneumoniae) & Atypical Pneumonia: (Legionella , Chlamydia) , intracellular pathogens : legionella & Mycobacteria

Drug	Mechanism of action	Spectrum	Adverse effects
Ciprofloxacin (most active against pseudomonas) , levofloxacin (superior activity against streptococcus pneumoniae) & Ofloxacin	Inhibit DNA gyrase (topoisomerase II) and topoisomerase IV, blocking DNA replication and transcription	Excellent against gram -ve : pseudomonas aeruginosa , Neisseria meningitis, Haemophilus , campylobacter <i>Moderate against gram +ve : staphylococcus but not MRSA</i>	1. Photosensitivity 2. QTc prolongation 3. Tendinitis , tendon rupture 4. Cartilage damage 5. Contraindicated in pregnancy
Gemifloxacin & Moxifloxacin	//	<i>Improved activity against gram +ve (streptococcus pneumoniae , some staphylococcus)</i> Atypical bacteria : Mycoplasma , chlamydia and legionella	//

Other drugs used in UTI

Drug	Mechanism of action	Spectrum	Adverse effects
Nitrofurantoin Should not be given to renal failure or < 1 month of age	Damages bacterial DNA	E.coli & enterococci Ineffective against : pseudomonas , proteus , klebsiella , enterobacter	Pulmonary fibrosis , pneumonitis , megaloblastic anemia , hemolysis in G6PD deficiency, polyneuropathies , brown urine discolouration
Methenamine Antagonize the action of sulfonamides	Converts to formaldehyde in acidic urine	Used only for chronic suppressive treatment of UTI caused by E. coli. Broad-spectrum antibiotics except urea-splitting proteus	Crystalluria Contraindicated in hepatic failure (ammonia generation)