

Trimethoprim

Trimethoprim is a bacteriostatic antibiotic that inhibits bacterial dihydrofolate reductase. This enzyme normally reduces dihydrofolic acid to tetrahydrofolic acid using NADPH as an electron donor. Inhibition of this enzyme leads to inhibition of the synthesis of tetrahydrofolic acid, which is essential in the synthesis of nucleotides for DNA synthesis. Trimethoprim is commonly used in combination with sulfamethoxazole, which is a sulfonamide antibiotic that is a competitive antagonist of PABA metabolite and causes inhibition of the enzyme dihydropteroate synthetase, also in the folic acid synthesis pathway. Using these drugs in combination causes sequential block of folate synthesis and has a synergistic effect. Trimethoprim is commonly used in the treatment of recurrent urinary tract infections and is also effective against *Shigella* and *Salmonella*. Specifically, TMP-SMX is used for both prophylaxis and treatment of *Pneumocystis jirovecii*. Use of this antibiotic can cause a decrease in red and white blood cell counts due to lowering of folic acid levels in the individual. This side effect can be alleviated with administration of leucovorin, also called folinic acid. Leucovorin is a derivative of tetrahydrofolic acid that has activity equivalent to that of folic acid. Leucovorin does not require dihydrofolate reductase for activation and is therefore not inhibited by drugs like trimethoprim.



PLAY PICMONIC

Mechanism of Action

Bacteriostatic

Bacteria-shocked

Bacteriostatic antibiotics limit the growth of bacteria by interfering with bacterial protein production, DNA replication, or other aspects of metabolism while not necessarily directly harming the organism. Upon removal of the bacteriostatic agent, the bacteria can regrow as opposed to bactericidal agents that directly kill bacteria.

Inhibits Bacterial Dihydrofolate Reductase

Di-hydryl-foliage Red-ducks

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Causes Sequential Block of Folate Synthesis

Foliage-trees destroyed

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Used in Combination with Sulfamethoxazole

SMX-snowmobile

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Combination Used For Recurrent Urinary Tract Infections

Urinary-tract-on-fire

Trimethoprim is commonly used in the treatment of recurrent urinary tract infections due to activity against *E. coli*, the most common cause of urinary tract infections.

Indications

Shigella

She-Jello

Shigella is a common cause of bacterial diarrhea worldwide. Transmission is via contaminated food and water, but also via direct person-to-person contact. *Shigella* has a high virulence; as few as 10 to 100 bacteria can cause disease because its organisms can survive the stomach's acidic conditions.

Salmonella

Salmon

Salmonella are classified within the Enterobacteriaceae family of the Gram negative bacilli. Salmonella is often classified into Salmonella typhi and nontyphoid Salmonella, mostly commonly Salmonella enteritidis. Salmonella enteritidis is a common cause of gastrointestinal disease in the US although antibiotics are preferably not given for this type of infection.

Pneumocystis Jiroveci Pneumonia

Nude-Mona-sisters in a Jeep

Pneumocystis jiroveci is a fungal infection which typically presents with hypoxia and fever in the lungs of immunocompromised patients. The infection is usually diagnosed using classic X-ray findings of diffuse interstitial infiltration bilaterally. Definitive diagnosis can be made using lavage or biopsy, where it can be identified by methenamine on silver stain. In order to prevent the disease in patients with HIV and CD4 counts below 200, TMP SMX is used prophylactically. TMP-SMX is also used as treatment for diagnosed disease.

Side Effects

Decrease in Red and White Blood Cells

Trees falling on and smashing Red and White Blood Cells

Use of this antibiotic can cause a decrease in red and white blood cell counts due to lowering of folic acid levels in the individual.

Alleviated with Leucovorin Rescue

Luke-on-vulture rescuing red and white blood cells

Decrease in red and white blood cell counts can be alleviated with administration of leucovorin, also called folinic acid. Leucovorin is a derivative of tetrahydrofolic acid that has activity equivalent to that of folic acid. Leucovorin does not require dihydrofolate reductase for activation and is therefore not inhibited by drugs like trimethoprim.