**NAME**: ALAGA AYODEJI

**DEPT:** ANATOMY

**MATRIC NO:** 18/MHS03/016

**LEVEL:** 300LVL

**COUSRE:** PHA 306: SYSTEMIC PHARMACOLOGY

**DATE:** 06-04-2020

**ASSIGNMENT SOLUTION:**

1. Name of the Drug

**Nitrofurantoin** is an antibacterial agent used in the treatment of urinary tract infections and causes brown coloration of urine. The Macrobid® brand of nitrofurantoin is a hard gelatin capsule shell containing the equivalent of 100 mg of nitrofurantoin in the form of 25 mg of nitrofurantoin macrocrystals and 75 mg of nitrofurantoin monohydrate.

1. Antibacterial Activity:

Nitrofurantoin is effective against many gram-positive and gram-negative organisms. Nitrofurantoin is bactericidal against most common urinary tract pathogens, including Escherichia coli, Enterococci, Klebsiella, Staphylococcus saprophyticus, and Enterobacter coli and Non-ESBL-producing E. coli strains.

1. Mechanism of Action

The mechanism of the antimicrobial action of nitrofurantoin is unusual among antibacterials. Nitrofurantoin is reduced by bacterial flavoproteins to reactive intermediates which inactivate or alter bacterial ribosomal proteins and other macromolecules. As a result of such inactivations, the vital biochemical processes of protein synthesis, aerobic energy metabolism, DNA synthesis, RNA synthesis, and cell wall synthesis are inhibited. Nitrofurantoin is bactericidal in urine at therapeutic doses. The broad-based nature of this mode of action may explain the lack of acquired bacterial resistance to nitrofurantoin, as the necessary multiple and simultaneous mutations of the target macromolecules would likely be lethal to the bacteria.

1. Pharmacokinetics:

Bioavailability is 80%, with roughly 25% of nitrofurantoin excreted in the urine unchanged. Excretion is complete within 6 hours after intake and urine concentrations of 200–400 µg/mL are achieved after a dose of 100 mg q8h.

1. Adverse Effects:

In clinical trials of Macrobid, the most frequent clinical adverse events that were reported as possibly or probably drug-related were nausea (8%), headache (6%): and flatulence (1.5%). Additional clinical adverse events reported as possibly or probably drug-related occurred in less than 1% of patients studied and are listed below within each body system in order of decreasing frequency:

* ***Gastrointestinal****:* Diarrhea, dyspepsia, abdominal pain, constipation, emesis
* ***Neurologic***: Dizziness, drowsiness, amblyopia
* ***Respiratory*:** Acute pulmonary hypersensitivity reaction
* ***Allergic***: Pruritus, urticaria
* ***Dermatologic*:** Alopecia
* ***Miscellaneous*:** Fever, chills, malaise
* ***Gastrointestinal***: Sialadenitis, pancreatitis. There have been sporadic reports of Pseudomembranous colitis with the use of nitrofurantoin. The onset of pseudomembranous colitis symptoms may occur during or after antimicrobial treatment.
* ***Neurologic*:** Peripheral neuropathy, which may become severe or irreversible, has occurred. Fatalities have been reported. Conditions such as renal impairment (creatinine clearance under 60 mL per minute or clinically significant elevated serum creatinine), anemia, diabetes mellitus, electrolyte imbalance, vitamin B deficiency, and debilitating diseases may increase the possibility of peripheral neuropathy. Asthenia, vertigo, and nystagmus also have been reported with the use of nitrofurantoin. Benign intracranial hypertension (pseudotumor cerebri), confusion, depression, optic neuritis, and psychotic reactions have been reported rarely. Bulging fontanels, as a sign of benign intracranial hypertension in infants, have been reported rarely.
* ***Respiratory***: Chronic, subacute, or acute pulmonary hypersensitivity reactions may occur with the use of nitrofurantoin. Chronic pulmonary reactions generally occur in patients who have received continuous treatment for six months or longer. malaise, dyspnea on exertion, cough, and altered pulmonary function are common manifestations which can occur insidiously. Radiologic and histologic findings of diffuse interstitial pneumonitis or fibrosis, or both, are also common manifestations of the chronic pulmonary reaction. Fever is rarely prominent. The severity of chronic pulmonary reactions and their degree of resolution appear to be related to the duration of therapy after the first clinical signs appear. Pulmonary function may be impaired permanently, even after cessation of therapy. the risk is greater when chronic pulmonary reactions are not recognized early.

In subacute pulmonary reactions, fever and eosinophilia occur less often than in the acute form. Upon cessation of therapy, recovery may require several months. If the symptoms are not recognized as being drug-related and nitrofurantoin therapy is not stopped, the symptoms may become more severe. Acute pulmonary reactions are commonly manifested by fever, chills, cough, chest pain, dyspnea, pulmonary infiltration with consolidation or pleural effusion on x-ray, and eosinophilia. Acute reactions usually occur within the first week of treatment and are reversible with cessation of therapy. Resolution often is dramatic. Changes in EKG (e.g., non-specific ST/T wave changes, bundle branch block) have been reported in association with pulmonary reactions. Cyanosis has been reported rarely.

* ***Hepatic*:** Hepatic reactions, including hepatitis, cholestatic jaundice, chronic active hepatitis, and hepatic necrosis, occur rarely.
* ***Dermatologic*:** Exfoliative dermatitis and erythema multiforme (including Stevens-Johnson syndrome) have been reported rarely.
* ***Hematologic***: Cyanosis secondary to methemoglobinemia has been reported rarely.