**NAME: AKHUEMONKHAN ESTHER ELIZABETH**

**MATRIC NUMBER:17/MHS06/014**

**300LEVEL**

**INTODUCTORY PHARMACOLOGY AND TOXICOLOGY II**

**A named bacterial protein synthesis inhibitor, stating its mechanism of action, indication for use, toxicity and adverse effects.**

**MACROLIDES e.g Erythromycin**

Erythromycin is an orally effective antibiotic used for the treatment of a number of bacterial infections discovered in 1952 in the metabolic products of a strain of Streptocyces erythreus, originally obtained from a soil sample.Erythromycin is a bacteriostatic antibiotic drug produced by a strain of Saccharopolyspora erythraea (formerly Streptomyces erythraeus) and belongs to the macrolide group of antibiotics which consists of Azithromycin, Clarithromycin, Spiramycin and others.

Erythromycin is widely used for treating a variety of infections, including those caused by gram-positive and gram-negative bacteria.It is available for administration in various forms, including intravenous, topical, and eye drop preparations.

**Mechanism of Action:**

Macrolides are inhibitors of protein synthesis.  They impair the elongation cycle of the peptidyl chain by specifically binding to the 50 S subunit of the ribosome.  Specificity towards prokaryotes relies upon the absence of 50S ribosomes in eukaryotes.

Erythromycin is a bacteriostatic antibiotic, which means it prevents the further growth of bacteria rather than directly destroying it. This action occurs by inhibiting protein synthesis.

Erythromycin displays bacteriostatic activity or inhibits growth of bacteria, especially at higher concentrations. By binding to the 50s subunit of the bacterial rRNA complex, protein synthesis and subsequent structure and function processes critical for life or replication are inhibited.

Erythromycin binds to the 23S ribosomal RNA molecule in the 50S subunit of the bacterial ribosome; this causes a blockage in the exiting of the peptide chain that is growing. Given that humans have the 40S and 60S subunits, and do not have 50S subunits, erythromycin does not affect protein synthesis in human tissues.

Resistance can develop against erythromycin. This occurs via modification of the 23S rRNA found in the 50S rRNA. The erythromycin cannot bind to the ribosome, and the bacteria can continue the process of protein synthesis.

Aside from being a bacteriostatic macrolide antibiotic, erythromycin is a pro-motility drug. It is an agonist to motilin, which increases motility in the gut.

Once erythromycin is orally administered, it gets deactivated by gastric acid. Oral tablets must either contain an ester or stable salt as part of the molecular structure or be enteric-coated. Following absorption via the gastrointestinal system, it diffuses into various tissues and phagocytes. As phagocytes circulate the blood and induce phagocytosis of harmful bacteria, erythromycin gets released during this process.

The liver metabolizes most of the administered erythromycin. It undergoes demethylation through the cytochrome P450 system, specifically the enzyme CYP3A4, and undergoes elimination through bile. A very small percentage of the drug undergoes renal excretion.

Erythromycin has a half-life of 1.5 to 2 hours. Levels of the drug peak 4 hours after intake.

**INDICATION FOR USE;**

Erythromycin is indicated in the treatment of infections caused by susceptible strains of various bacteria. The indications for erythromycin have been summarized by body system below:

**- Respiratory infections**

Mild to moderate upper respiratory tract infections caused by Streptococcus pyogenes, Streptococcus pneumoniae, or Haemophilus influenzae (when used concomitantly with appropriate doses of sulfonamides) can be treated with erythromycin.Mild to moderate lower-respiratory tract infections due to susceptible strains of Streptococcus pneumoniae or Streptococcus pyogenes may also be treated. Erythromycin treats listeriosis caused by Listeria monocytogenes may also be treated with erythromycin. Erythromycin is indicated to treat pertussis (whooping cough) caused by Bordetella pertussis. It is effective in eliminating the causative organism from the nasopharynx of infected individuals, rendering them noninfectious. Clinical studies suggest that erythromycin may aid in the prevention of pertussis infection for individuals who have been exposed to the bacteria. Respiratory tract infections due to Mycoplasma pneumoniae may also be treated with erythromycin. Despite the fact that no controlled clinical efficacy studies have been conducted to this date, in vitro and certain preliminary clinical study results indicate that erythromycin may be an effective treatment in Legionnaires’ Disease. Finally, erythromycin is indicated to treat diphtheria and other infections due to Corynebacterium diphtheriae, as an adjunct to antitoxin, to prevent carrier status and to eradicate the organism in existing carriers. In addition to the prevention of diphtheria, erythromycin can be used to prevent rheumatic fever in penicillin intolerant patients.

**- Skin infections**

Mild to moderate skin or skin structure infections caused by Streptococcus pyogenes or Staphylococcus aureus may be treated with erythromycin, however, resistant staphylococcal organisms may emerge. Erythromycin can also be used to treat erythrasma, an infectious condition caused by Corynebacterium minutissimum.

**- Gastrointestinal infections**

Intestinal amebiasis caused by Entamoeba histolytica can be treated with oral erythromycin. Extraenteric amebiasis warrants treatment with other antimicrobial drugs.

**- Genital infections/STIs**

Erythromycin can be used as an alternative drug in treating acute pelvic inflammatory disease caused by N. gonorrheae in female patients who have demonstrated hypersensitivity or intolerance to penicillin. Syphilis, caused by Treponema pallidum, can be treated with erythromycin. It serves as an alternative treatment for primary syphilis in patients who have demonstrated penicillin hypersensitivity. Erythromycin can also be used in the primary stage of primary syphilis.Another approved indication of erythromycin is to treat chlamydial infections that cause conjunctivitis of the newborn, pneumonia of infancy, and urogenital infections occurring in pregnancy. It is indicated as an alternative option to tetracyclines for the treatment of uncomplicated rectal, urethral and endocervical infections in adults caused by Chlamydia trachomatis. Erythromycin can be used in nongonococcal urethritis can be used when tetracyclines cannot be administered. Finally, erythromycin is indicated to treat nongonococcal urethritis due to Ureaplasma urealyticum.

**TOXICITY**:

Macrolide antibiotics have varying levels of cardiotoxicity. Erythromycin carries the most prominent risk of cardiotoxicity among the more commonly used macrolide antibiotics. It induces QT prolongation and increases the risk of the potentially deadly heart rhythm known as torsades de pointes. Careful monitoring of the QTc interval on the ECG is recommended to minimize risk. Patients at higher risk should also have their potassium, magnesium, and calcium levels monitored.

There is no known reversal agent for erythromycin.

**ADVERSE EFFECTS**:

All antibiotics carry a significant risk of nausea, vomiting, abdominal pain, and diarrhea. Erythromycin is a motilin agonist, and this increases the likelihood of gastrointestinal side effects compared to other antibiotics.

All macrolide antibiotics cause QT prolongation. Azithromycin causes the least QT prolongation, usually clinically insignificant. Clarithromycin causes greater QT prolongation. Erythromycin is known to cause major prolongation of the QT interval and carries a risk of torsades de pointes. This arrhythmia may cease on its own, or it may degenerate into ventricular fibrillation, a deadly heart rhythm.

There also exists a risk of rash, allergic reaction, and reversible deafness. Rare side effects include Stevens-Johnson syndrome, toxic epidermal necrolysis, and cholestasis.

Erythromycin comes in various forms. Pregnant women should not use the form of erythromycin estolate as it may cause hepatotoxicity. It may also increase the risk of pyloric stenosis in the newborn.

Erythromycin is a cytochrome P450 inhibitor; this means it carries the potential to interact with broad ranges of medications. Given it is an inhibitor of CYP450, drugs that get metabolized via the cytochrome P450 system would have increased concentrations and hence carry risks of toxicity.