**CARBAPENEMS**

**Imipenem** is an extremely potent and broads pectrum β-lactam antibiotic whose range of activity includes gram-positive cocci, Enterobacteriaceae, *Ps. aeruginosa, Listeria* as well as anaerobes like *Bact. fragilis* and *Cl.difficile*. It is resistant to most β-lactamases;inhibits penicillinase producing staphylococci.

Imipenem-cilastatin 0.5 g i.v. 6 hourly (max 4 g/day) has proved effective in a wide range of serious hospital-acquired respiratory, urinary, abdominal, pelvic, skin and soft tissue infections including those in neutropenic, cancer and AIDS patients. For *Ps. aeruginosa* infections, it should be combined with gentamicin.

**Side effect**

Imipenem has propensity to induce seizures at higher doses and in predisposed patients.

Diarrhoea, vomiting, skin rashes and other hypersensitivity reactions are the side effects.

**TETRACYCLINES** (Broad-Spectrum Antibiotics)



These are a class of antibiotics having a nucleus of four cyclic rings. All are obtained from soil actinomycetes

All tetracyclines are slightly bitter solids which are slightly water soluble, but their hydrochlorides are more soluble. Aqueous solutions are unstable. All have practically the same antimicrobial activity (with minor differences).

Tetracycline, Doxycycline, Oxytetracycline, Minocycline and Demeclocycline.

**Mechanism of action**

The tetracyclines are primarily bacteriostatic; inhibit protein synthesis and will inhibit microorganism growth.

**Antimicrobial spectrum**

tetracyclines inhibited practically all types of pathogenic microorganisms except fungi and viruses; hence the name ‘broad-spectrum antibiotic.

Uses of tetracyclines;

(a) *Venereal diseases:*

• *Chlamydial nonspecific urethritis/endocervicitis:* 7 day doxycycline treatment is aseffective as azithromycin single dose.

(b) *Atypical pneumonia:* due to *Mycoplasma pneumoniae:* duration of illness is reduced bytetracycline therapy. Psittacosis is treated in 2 weeks by tetracyclines.

(c) *Cholera:* Tetracyclines have adjuvant value by reducing stool volume and limiting the duration of diarrhoea.

(d) *Brucellosis:* Tetracyclines are highly efficacious; cause rapid symptomatic relief; therapy.

**Adverse effects**

* Discoloration of teeth and enamel hypoplasia (young children)
* [Diarrhea](https://www.rxlist.com/script/main/art.asp?articlekey=2985), [Nausea](https://www.rxlist.com/script/main/art.asp?articlekey=4510), [Photosensitivity](https://www.rxlist.com/script/main/art.asp?articlekey=4883), Stomach upset, Loss of appetite
* White patches or sores inside your [mouth](https://www.rxlist.com/script/main/art.asp?articlekey=33422) or on your [lips](https://www.rxlist.com/script/main/art.asp?articlekey=4173)
* [Swollen tongue](https://www.rxlist.com/script/main/art.asp?articlekey=97582)
* Black hairy [tongue](https://www.rxlist.com/script/main/art.asp?articlekey=9075), [Dizziness](https://www.rxlist.com/script/main/art.asp?articlekey=6114), [Headache](https://www.rxlist.com/script/main/art.asp?articlekey=11396)

**Contraindications**

* Hypersensitivity
* Severe [hepatic](https://www.rxlist.com/script/main/art.asp?articlekey=3704) [dysfunction](https://www.rxlist.com/script/main/art.asp?articlekey=13498)
* Pregnancy
* Children under 6 years

**Aminoglycosides**

*Aminoglycosides* provide effective bactericidal activity against:

• gram-negative bacilli

• some aerobic gram-positive bacteria

• mycobacteria

**Common aminoglycosides**

Aminoglycosides currently in use include:

• amikacin sulfate

• gentamicin sulfate

• kanamycin sulfate

• neomycin sulfate

• paromomycin sulfate

• streptomycin sulfate

• tobramycin sulfate.

**Pharmacokinetics**

Because aminoglycosides are absorbed poorly from the GI tract, they’re usually given parenterally. After I.V. or I.M. administration aminoglycoside absorption is rapid and complete.

***Distribution***

Aminoglycosides are distributed widely in extracellular fluid They readily cross the placental barrier, but don’t cross the blood brain barrier.

***Metabolism and excretion***

Aminoglycosides aren’t metabolized. They’re excreted primarily unchanged by the kidneys

**Mechanism of action**

Aminoglycosides act as bactericidal drugs (this means they kill bacteria) against susceptible organisms by binding to the bacterium’s 30S subunit, a specific ribosome in the microorganism, thereby interrupting protein synthesis and causing the bacterium to die.

**Uses of aminoglycosides**

Aminoglycosides are most useful in treating:

• infections caused by gram-negative bacilli

• serious nosocomial (hospital-acquired) infections, such as gram-negative bacteremia, peritonitis (inflammation of the peritoneum, the membrane that lines the abdominal cavity), and pneumonia, in critically ill patients

• urinary tract infections (UTIs) caused by enteric bacilli that are resistant to less toxic antibiotics, such as penicillins and

cephalosporins

• infections of the central nervous system (CNS) and the eye (treated with local instillation).

**Drug interactions**

Carbenicillin and ticarcillin reduce the effects of amikacin, gentamicin, kanamycin, neomycin, streptomycin, and tobramycin. This is especially true if the penicillin and aminoglycoside are mixed in the same container or I.V. line.

-Amikacin, gentamicin, kanamycin, neomycin, streptomycin, and tobramycin administered with neuromuscular blockers increase neuromuscular blockade, resulting in increased muscle relaxation and respiratory distress.

**Side effects**

1. Toxicity to the kidneys may result in renal failure; toxicity to the neurologic system results in peripheral neuropathy with numbness and tingling of the extremities. The risk of renal toxicity also increases when amikacin, gentamicin, kanamycin, or tobramycin is taken with cyclosporine, amphotericin B, or acyclovir.
2. The symptoms of ototoxicity (damage to the ear) caused by aminoglycosides may be masked by antiemetic drugs. Loop diuretics taken with aminoglycosides increase the risk of ototoxicity. Hearing loss may occur in varying degrees and may be irreversible.

**Contraindications**

The drugs are contraindicated in pregnant women and patients with renal failure.

**Macrolides**

*Macrolides* are bacteriostatic drugs used to treat a number of common infections.

They include erythromycin and its derivatives, azithromycin and clarithromycin.

**Pharmacokinetics**

Because erythromycin is acid-sensitive, it must be buffered or have an enteric coating to prevent destruction by gastric acid. Erythromycin is absorbed in the duodenum. It’s distributed to most tissues and body fluids except, in most cases, for cerebrospinal fluid (CSF). However, as a class, macrolides can enter the CSF when meninges are inflamed.

***Metabolism and excretion***

Erythromycin is metabolized by the liver and excreted in bile in high concentrations; small amounts are excreted in urine. It also crosses the placental barrier and is secreted in breast milk.

**Mechanism of action**

Macrolides inhibit ribonucleic acid (RNA)–dependent protein synthesis by acting on a small portion of the ribosome, and this lead to bacterial death.

**Uses**

**Erythromycin** has a range of therapeutic uses.

• It provides a broad spectrum of antimicrobial activity against gram-positive and gram-negative bacteria, including *Mycobacterium,* *Treponema, Mycoplasma,* and *Chlamydia.*

• It’s also effective against pneumococci and group A streptococci. *Staphylococcus aureus* is sensitive to erythromycin; however, resistant strains may appear during therapy.

• Erythromycin is the drug of choice for treating *Mycoplasma pneumoniae* infections as well as pneumonia caused by *Legionella pneumophila.*

**Azithromycin** provides a broad spectrum of antimicrobial activity against gram-positive and gram-negative bacteria, including *Mycobacterium,* *S. aureus, Haemophilus influenzae, Moraxella catarrhalis,* and *Chlamydia.* It’s also effective against pneumococci and groups C, F, and G streptococci.

**Clarithromycin** is a broad-spectrum antibacterial that’s active against gram-positive aerobes, such as *S. aureus, S. pneumoniae,* and *Streptococcus pyogenes;* gram-negative aerobes, such as *H. influenzae* and *M. catarrhalis;* and other aerobes such as *M. pneumoniae.* Clarithromycin has also been used in combination with antacids, histamine-2 blockers, and proton pump inhibitors to treat *Helicobacter pylori*–induced duodenal ulcer disease.

**Fluoroquinolones**

*Fluoroquinolones* are structurally similar synthetic antibiotics. They are primarily administered to treat UTIs, upper respiratory tract infections, pneumonia, and gonorrhea and include:

• ciprofloxacin • levofloxacin • moxifloxacin

• norfloxacin • ofloxacin.

**Pharmacokinetics**

After oral administration, fluoroquinolones are absorbed well.

**Pharmacodynamics**

Fluoroquinolones interrupt deoxyribonucleic acid (DNA) synthesis during bacterial replication by inhibiting DNA gyrase, an essential enzyme of replicating DNA. As a result, the bacteria can’t reproduce.

**Pharmacotherapeutics**

Fluoroquinolones can be used to treat many UTIs. Each drug in this class also has specific indications.

**256**

• Ciprofloxacin is used to treat lower respiratory tract infections, infectious diarrhea, and skin, bone, and joint infections.

• Levofloxacin is indicated for the treatment of lower respiratory tract infections, skin infections, and UTIs.

• Moxifloxacin is used to treat acute bacterial sinusitis and mild to moderate community-acquired pneumonia.

• Norfloxacin is used to treat UTIs and prostatitis.

• Ofloxacin is used to treat selected sexually transmitted diseases, lower respiratory tract infections, skin and skin-structure

infections, and prostatitis (inflammation of the prostate gland).

**Adverse reactions to fluoroquinolones**

Fluoroquinolones are well tolerated by most patients, but some serious adverse effects may occur, including:

• dizziness • nausea and vomiting • diarrhea • abdominal pain.

**Serious reactions**

Moderate to severe phototoxic reactions have occurred with direct and indirect sunlight and with artificial ultraviolet

lights, with and without sunscreen. Light should be avoided for several days after stopping fluoroquinolone