Penicillins

Penicillins are **beta-lactam antibiotics** that inhibit the formation of peptidoglycan cross-links — links that are necessary for the integrity and viability of the bacteria.

10% of people report an allergy to penicillin, though 90% of this group are not allergic at all — the figure is thought to be 0.03%.

Natural	β-Lactamase Resistant	Amino-	Carboxy-	Ureido-
Penicillin G* Penicillin V**	Methicillin Nafcillin Oxacillin Cloxacillin Dicloxacillin Flucloxacillin	Ampicillin Amoxicillin	Carbenicillin Ticarcillin	Mezlocillin Piperacillin

General Points

Pen G. and Pen V. are active against many gram positives, but a limited range of gram negative bacteria.

(Piv)mecillinam is only active against gram-negatives, primarily used in the treatment of UTIs.

Aminopenicillins are extended spectrum, but less effective than Pen G. against gram-positive cocci.

Clavulanic acid has no antibacterial activity, but is a potent inhibitor of beta-lactamase.

Adverse Effects

Nausea, Vomiting

Hypersensitivity Reactions

Neutropenia/Eosinophilia

Clostridium difficile colitis

Cholestatic jaundice

* *Benzylpenicillin* ** *Phenoxymethyl Penicillin*

Lincosamides

Lincosamides are a class of antibiotics that work by interfering with protein synthesis, specifically by binding to the **23s portion of the 50s subunit** of bacterial ribosomes.

The first discovered lincosamide — **lincomycin** — was isolated from the *Streptomyces lincolnensis* strain, its name deriving from the soil sample taken from Lincoln, Nebraska.

Clinically Approved Lincosamides

Lincomycin | Clindamycin

General Points

Lincomycin is **narrow spectrum** in effect, mostly used for gram-positive infections. It is available **IM** and **IV**.

Clindamycin is available orally, topically, IV and intravaginally. Mostly used to treat **anaerobic gram-negative** infections, but may be used against some gram-positive cocci.

Clindamycin **may prolong effects** of neuromuscular blocking drugs such as vecuronium.

Adverse Effects

Nausea, Vomiting
Abdominal Pain, Cramps
Rash, Metallic Taste

Clindamycin is also associated with *Clostridium difficile*-associated diarrhoea.

Carbapenems

Carbapenems are a class of **beta-lactam antibiotics** with a broad spectrum of bactericidal activity - their structure renders them **highly resistant** to beta-lactamases.

Imipenem can be hydrolysed in the kidney by the enzyme **dehydropeptidase 1**, hence why it is given with an inhibitor of dehydropeptidase — **cilastatin.**

Clinically Approved Carbapenems

Imipenem	Meropenem	Ertapenem	Doripenem

General Points

All are given by **IV and IM** routes, except meropenem, which is only IV. At high doses, imipenem is **seizuregenic.**

Doripenem is particularly active against *Pseudomonas aeruginosa*, compared to ertapenem which is not.

Meropenem is bactericidal, **except** against *Listeria monocytogenes*, where it is bacteriostatic.

Marketing slogan of ertapenem is **The Power of One**, as the dose is 1g once daily.

Pharmacokinetics

Carbapenems have **short half-lives** — between 1-5hrs.

Primarily undergo **renal** metabolism.

Glycopeptides

Glycopeptide antibiotics are a class of drugs of microbial origin, which work by inhibiting peptidoglycan synthesis — the antecedent of cell walls.

These drugs are principally effective against **gram-positive cocci**, exhibit a **narrow spectrum** of action, **bactericidal** only against enterococci and tend to be used in those who are either critically ill, hypersensitive to β-lactams, or infected with β-lactam-resistant species.

Clinically Approved Glycopeptides

Vancomycin	Teicoplanin	Telavancin

General Points

All three are given by **IV** due to poor absorption, though vancomycin may be given orally to treat pseudomembranous colitis. Teicoplanin may be given IM.

Vancomycin should be administered both dilute and slowly, to avoid **red man syndrome.**

Telavancin is associated with a higher rate of kidney failure than vancomycin.

Adverse Effects

Ototoxicity
Nephrotoxicity (enhanced with aminoglycosides)
Thrombophlebitis at injection site
Rash
Neutropenia/Thrombocytopenia
Nausea

Thionamides

Carbimazole **Propylthiouracil**

Thionamides
- Used to treat hyperthyroidism and Graves disease.
- Inhibit thyroxine peroxidase which, in turn, inhibits thyroid hormone.

Given that T_4 has a long half-life, it may take up to **6 weeks** for circulating T_4 and T_3 concentrations to return to normal. Both drugs accumulate in the thyroid gland over time, meaning their duration of action is longer than half-life expectations.

Carbimazole is converted by first-pass metabolism into the active ingredient **methimazole**. Methimazole has a short half-life of around 3-5 hours.

Propylthiouracil has 1/10 the activity of methimazole — usually reserved for those intolerant to carbimazole. **Cross-sensitivity** occurs between carbimazole and propylthiouracil.

Unwanted effects include GI upset, headache, arthralgia and pruritic rash common in first 8 weeks. **Bone marrow suppression** may also occur.