

Penicillin

Penicillin belongs to the group of beta-lactam antibiotics. Its name is derived from the fungus (Brush, *Penicillium*), from which they were first obtained. This antibiotic was discovered by Alexander Fleming in 1928.

Antimicrobial spectrum

Narrow-spectrum penicillins (basic, natural) – effective against G+ bacteria and G– cocci (meningococci, gonococci) ^[1], oxacillin acts only against *Staphylococcus aureus* and partly against streptococci,

Broad-spectrum penicillins – effective against both G+ and G–.

Pharmacokinetics and pharmacodynamics

After **parenteral administration**, they are rapidly and completely absorbed. I.V. administration is preferred over i.m. (especially high doses), which is painful. Absorption after **oral administration** varies with penicillins, depending on the resistance to the acidic environment (pH of gastric juice). To minimize losses due to their adsorption in food, it is recommended to administer at least 1 hour before or after meal. Bioavailability is usually higher than 60 %. Plasma protein binding ranges from 18 % (amoxicillin) to 94 % (oxacillin), but only the unbound fraction is antimicrobially effective.

Penicillins are easily distributed into the extracellular fluid, due to their low liposolubility **they do not penetrate the cells**. They penetrate the blood-brain barrier poorly. Inflammatory meningeal changes facilitate their penetration into the CNS.

Most of the absorbed amount is **excreted in the urine**, by tubular secretion (90 %). This route of excretion may be inhibited by probenecid. 30–50 % of amount of penicillins present in the blood is excreted in breast milk. The biological **half-life is short** (about 1 hour).

Penicillins have a concentration-independent but **time-dependent** effect. At least 40 % of the dosing interval time, the antibiotic concentration should be higher than the minimum inhibitory concentration.^[1] They have no post-antibiotic effect.

Side effects and toxicity^[2]

Penicillins are **very safe** drugs. The most common side effect is allergic reactions (I-IV). They occur in approximately 1-10% of patients. Rarely, an anaphylactic reaction (0,05 %) may occur, which occurs 15-30 minutes after administration (most often i.v.). Anaphylaxis usually occurs after previous sensitization. **Late allergic manifestations** include urticaria, fever, joint pain, skin efflorescence, angioneurotic edema, interstitial nephritis (autoimmune reactions to the penicillin-protein complex), serum sickness, hemolytic anemia but also very serious complications such as Lyell's or Stevens-Johnson syndrome.

When aminopenicillins are administered to patients with infectious mononucleosis or lymphatic leukemia, a morbilliform rash may occur, which is a toxic reaction, not an allergic one. All penicillins have the ability to cause a cross-reaction, whether they are contained in food (milk from cows treated for mastitis) or in cosmetics. The allergic reaction to penicillins can be reduced by the administration of glucocorticoids.

Oral administration of penicillins can lead to dyspeptic problems – nausea, vomiting and diarrhea (especially with broad-spectrum penicillins). Diarrhea, even pseudomembranous colitis rarely occurs in broad-spectrum penicillins as a result of dysmicrobia.

Hoigné syndrome may occur as unusual side effects. It is induced in some patients after the administration of *procaine penicillin*. The clinical picture can quickly disappear, other times the psychological symptoms persist for many months. It retreats spontaneously. The syndrome is not a contraindication to repeated administration of penicillin. **Nicolau's syndrome** can also arise, as a result of incorrect administration techniques, in this case intraarterially. The symptoms depend on the type of organ affected.

The direct toxic effect of penicillins affects the CNS. Penicillins increase the irritability of neuron. It is used in experimental pharmacology for the intracerebral administration of penicillin to induce epilepsy in small laboratory animals and for the testing of antiepileptics. For this reason, we avoid intrathecal administration of penicillins. A direct effect on the CNS may occur even after administration so high (MIU) doses, especially in inflammatory meninx or reduced renal excretion.

Indications and contraindications^[2]

We usually use penicillins for treatment of respiratory infections, in the empirical therapy of community-acquired infections, in the treatment of nosocomial infections.

They are often combined with aminoglycosides.^[1] Interactions with other drugs are rare.

Penicillin allergies and increased seizures are contraindicated. High Na⁺ and K⁺ levels should be considered in cardiac and renal impairment.

Overview of penicillins

basic penicillins	penicilin G, penicilin V	
antistaphylococcal penicillins	oxacillin, cloxacillin, dicloxacillin, flucloxacillin	
broad-spectrum penicillins	aminopenicillins	ampicillin, amoxicillin
	carboxypenicillins	ticarcillin
	acylureidopenicillins	piperacillin

Basic penicillins

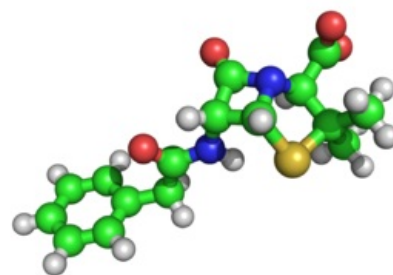
They include a group of acid-labile and acid-stable penicillins of narrow antimicrobial spectrum.

Template:HVLP (benzylpenicilin)^{[2][1]}

Penicillin G

It is not acid-resistant and therefore is not absorbed after oral administration, therefore it must be administered parenterally. It is not resistant to β -laktamases. It works against both G⁺ and G⁻ bacteria.

We use it as a drug of first choice in the treatment of infections caused by pneumococci, streptococci, meningococci, gonococci and staphylococci not producing β -laktamase, *Bacillus anthracis* and other G⁺ microorganisms, *Treponema pallidum* (syphilis) and other spirochetes, clostridia, actinomycetes, listeria a *Bacteroides* (s výjimkou *B. fragilis*), some Borrelia (a drug of first choice for Lyme disease). It is therefore used in the treatment of gonorrhea, diphtheria, measles, tonsillitis, erysipelas, rheumatic fever, leptospirosis. Some anaerobes are also sensitive.



Penicilin

- **Crystalline benzylpenicillin** – aqueous solution of potassium or sodium salt, well soluble in water for **i.v.** administration (infusion), first-line drug for meningococcal meningitis, pneumococcal pneumonia, *S. pyogenes*, clostridial infections, actinomycetes.
- **Procaine-benzylpenicillin** – suspension for **i.m.** administration (cannot be administered by i.v.), procaine increases the size of the molecule and thus prolongs the absorption and persistence of plasma concentrations, the drug of first choice for sleeping sores and streptococcal tonsillopharyngitis.
- **Benzatin-benzylpenicillin^[2]** – suspension with very low solubility in water, intended for strictly **i.m.** administration. It is absorbed very slowly, reaching low plasma concentrations that persist for a long time (up to 10 days). It is suitable for the treatment of acute nasopharyngitis caused by beta-hemolytic streptococci, as a prevention of rheumatic endocarditis.

The usual dose is 2-30 mil. IU. every 4-6 hours in the infusion (0,5 mil. IU)^[3] Increased potassium intake should be expected when benzylpenicillin potassium is administered.

Template:HVLP (phenoxymethylpenicillin)^{[2][1]}

Penicillin V

Acid-resistant (potassium salt), therefore, is not inactivated in the acidic environment of the stomach, so it can be administered orally. Bioavailability is about 60 %. Within 6 hours, its level reaches the limit of effectiveness.

The same antimicrobial spectrum as penicillin G is not resistant to β -laktamases. The drug of first choice for streptococcal tonsillopharyngitis (in case of allergy it is replaced by macrolides). Absorption from the GIT is not completely complete, so it is used for mild infections with sensitive bacteria (eg. sinusitis, otitis media, nasopharyngitis, erysipelas, measles, Lyme disease, prophylaxis endocarditis, periodontal and other dental infections).

Antistaphylococcal penicillins

These penicillins are resistant to staphylococcal β -laktamases. Their spectrum of action is staphylococci and streptococci. They are used where other penicillins are not effective.

Isoazolylpenicillins



Ospen®, a mass-produced medicinal product with phenoxymethylpenicillinTemplate:HVLP

Oxacillin

They are given orally for less severe staphylococcal infections. Oxacillin is usually indicated when penicillin-resistant staphylococci are detected. Recently, the resistance of staphylococci (*Staphylococcus aureus*, *Staphylococcus epidermidis*) to oxacillin (MRSA) has been increasing.

Methoxyphenicillins

Methicillin

It is not registered in the Czech Republic. It is considered a standard antistaphylococcal antibiotic worldwide. In the acidic environment of the stomach, it is inactivated, so it is usually administered only parenterally. Efficacy against staphylococci is identical to oxacillin.

Broad-spectrum penicillins^{[2][1][4][5]}

It differs from basic penicillins by a wider antimicrobial spectrum, which can be extended even more in combination with beta-lactamase inhibitors. Use in common respiratory tract infections, urinary tract infections, skin and soft tissue infections caused by eg. *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria catarrhalis*.

Aminopenicillins

Acid-resistant, semisynthetic antibiotic, not resistant to beta-lactamases. More effective on *Enterococcus spp.* and *Listeria monocytogenes*.

Ampicillin

Empirical treatment of community bacterial respiratory infections, urinary tract, typhoid fever, septic salmonella, listeriosis and meningitis. Absorption is limited by food, administered on an empty stomach, and may be administered by i.m.

Amoxicillin

The ampicillin analogue, a broader spectrum of action, produces higher serum levels. The advantage is complete absorption after oral administration, which is not limited by food. Part of regimens eradicating *Helicobacter pylori*.

Carboxypenicillins

The broad spectrum of action, partly against *Pseudomonas aeruginosa*, is not resistant to β -lactamases. Currently, no representative is registered in the Czech Republic.

Ticarcillin

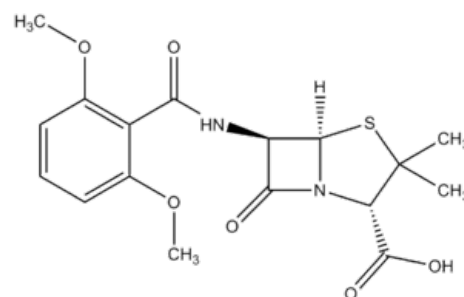
Effective on G- microbes that are resistant to ampicillin. It is often combined with beta-lactamase inhibitors and combined with aminoglycosides (because resistance develops rapidly in monotherapy). It is administered only i.v.

Acylureidopenicillins

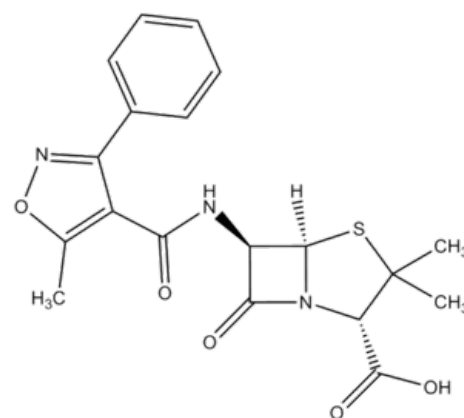
The spectrum of action is even wider than ticarcillin, they are not resistant to β -lactamases.

Piperacillin

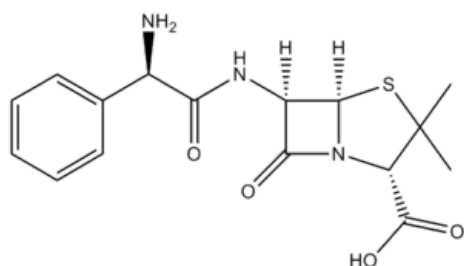
It is often combined with tazobactam. The product is effective against both G+ and G- bacteria, including nosocomial pathogens. It acts on *Bacteroides sp.* and *Clostridia sp.*, do not affect MRSA. In severe infections, their effect is enhanced by combination with aminoglycosides.



Methicillin



Oxacillin



Ampicillin

Links

related articles

- Antibiotics
- Beta-lactam antibiotics

External links

- <https://www1.lf1.cuni.cz/~hrozs/Atb2011/antibio02.htm>
- Peniciliny (česká wikipedie)
- Penicillin (anglická wikipedie)

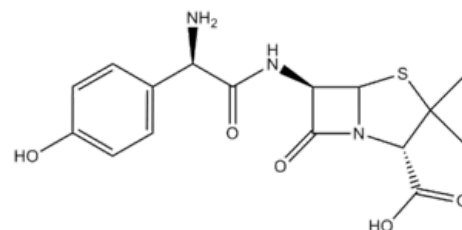
Source

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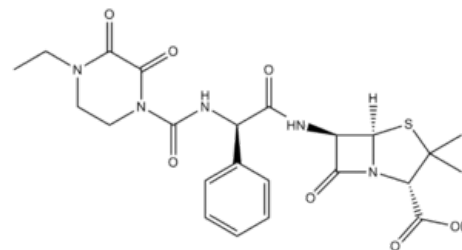
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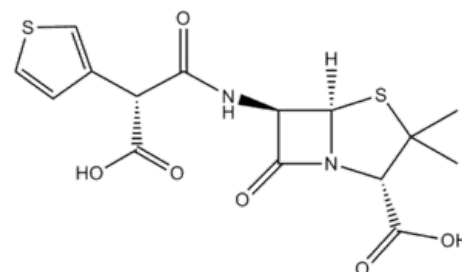
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Amoxicillin



Piperacillin



Tikarcilin