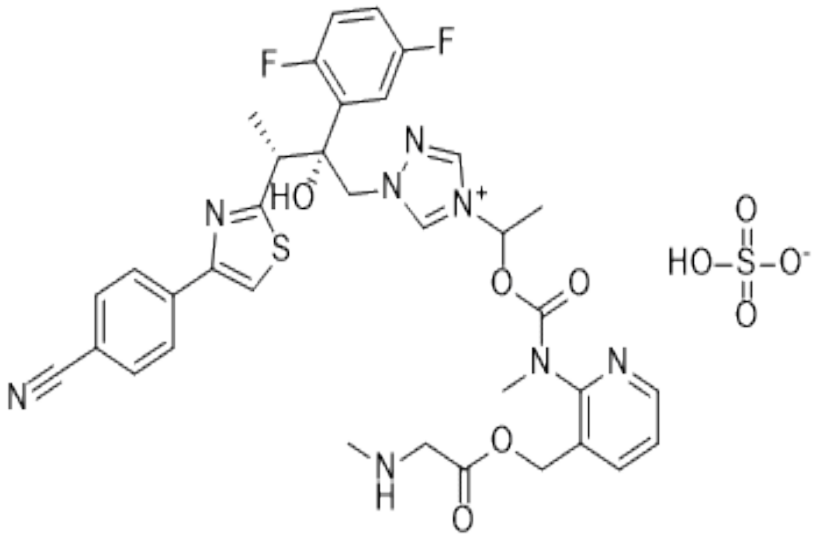
26. Isavuconazonium

Isavuconazonium sulfate (BAL8557; trade name Cresemba) is a prodrug for isavuconazole which is a triazole antifungal agent. **Isavuconazonium** is used to treat invasive aspergillosis and invasive mucormycosis.

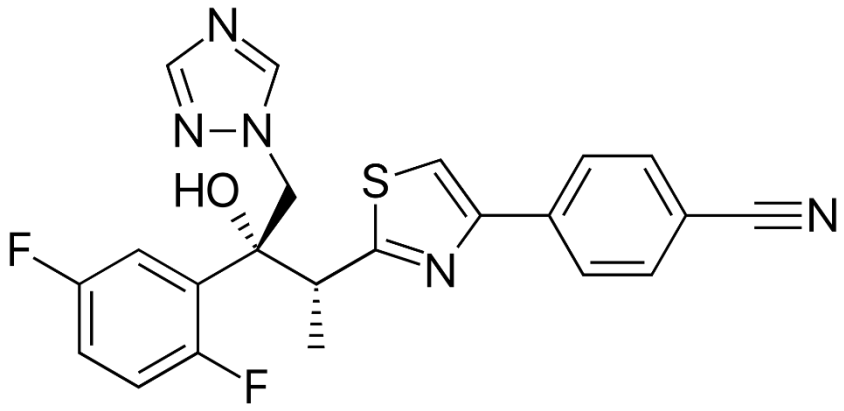
Isavuconazonium is a triazole antifungal agent used primarily in the treatment of invasive aspergillosis and mucormycosis infections. **Isavuconazonium** is associated with a low rate of transient and asymptomatic serum aminotransferase elevations during therapy,

Isavuconazonium is a second-generation triazole antifungal approved on March 6, 2015 by the FDA for the treatment of invasive aspergillosis and invasive mucormycosis, marketed by Astellas under the brand Cresemba. It is the prodrug form of isavuconazole, the active moiety, and it is available in oral and parenteral



Isavuconazole is a new extended-spectrum triazole with activity against yeasts, molds, and dimorphic fungi. It is approved for the treatment of invasive aspergillosis and mucormycosis. Advantages of this triazole include the availability of a water-soluble intravenous formulation, excellent bioavailability of the oral formulation, and predictable pharmacokinetics in adults

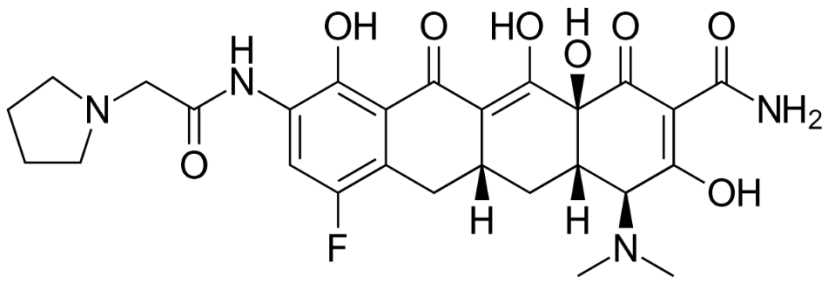
Isovuconazole



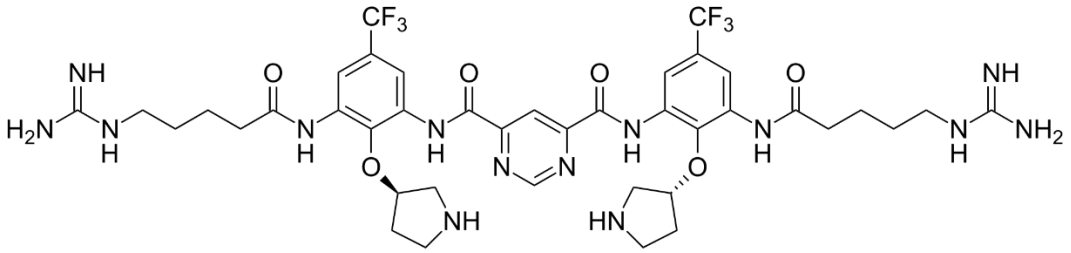
27. Eravacycline

Eravacycline (TP-434) is a synthetic halogenated tetracycline class antibiotic in development by Tetraphase Pharmaceuticals. It is closely related to tigecycline. It has a broad spectrum of activity including many multi-drug resistant strains of bacteria.

Eravacycline (TP-434 or 7-fluoro-9-pyrrolidinoacetamido-6-demethyl-6-deoxytetracycline) is a novel fluorocycline that was evaluated for antimicrobial activity against panels of recently isolated aerobic and anaerobic Gram-negative and Gram-positive bacteria.



28. Brilacidin



Brilacidin is under investigation for the supportive care of Mucositis, Stomatitis, Mouth Diseases, and Head and Neck Neoplasms. This compound belongs to the class of organic compounds known as aromatic anilides. These are aromatic compounds containing an anilide group in which the carboxamide group is substituted with an aromatic group. They have the general structure RNC(=O)R', where R= benzene, and R = aryl group.

ANTIBIOTICS AGAINST RESISTANCE MECHANISM

To stop the antibiotic from reaching its target bacteria may

- **Pump the antibiotic out from the bacterial cell.** Bacteria can produce pumps that sit in their membrane or cell wall. These so-called efflux pumps are very common in bacteria and can transport a variety of compounds such as signal molecules and nutrients. Some of these pumps can also transport antibiotics out from the bacterium, in this way lowering the antibiotic concentration inside the bacterial cell. In some cases mutations in the bacterial DNA can make the bacteria produce more of a certain pump, which in turn increases resistance.
- **Decrease permeability of the membrane that surrounds the bacterial cell.** Certain changes in the bacterial membrane make it more difficult to pass through. In this way, less of the antibiotic gets into the bacteria.
- **Destroy the antibiotic.** There are bacterial enzymes that can inactivate antibiotics. One example is β-lactamase that destroys the active component (the β-lactam ring) of penicillins, extremely important antibiotics for treating human infections. In later years, bacteria that produce extended-spectrum β-lactamases, so called ESBL-producing bacteria, have become a major problem. They can degrade a wide spectrum of β-lactam antibiotics, sometimes also the last resort drugs available for infections with these bacteria.

- **Modify the antibiotic.** Bacteria can sometimes produce enzymes that are capable of adding different chemical groups to antibiotics. This in turn prohibits binding between the antibiotic and its target in the bacterial cell.

- **Camouflage the target.** Changes in the composition or structure of the target in the bacterium (resulting from mutations in the bacterial DNA) can stop the antibiotic from interacting with the target. Alternatively, the bacteria can add different chemical groups to the target structure, in this way shielding it from the antibiotic.
- **Express alternative proteins.** Some bacteria are able to produce alternative proteins that can be used instead of the ones that are inhibited by the antibiotic. For example, the bacterium *Staphylococcus aureus* can acquire the resistance gene *mecA*and produce a new penicillin-binding protein. These proteins are needed for bacterial cell wall synthesis and are the targets of β-lactam antibiotics. The new penicillin-binding protein has low affinity to β-lactam antibiotics and is thus resistant to the drugs, and the bacteria survive treatment. This type of resistance is the basis in MRSA (methicillin-resistant *Staphylococcus aureus*).
- **Reprogram target.** Sometimes bacteria can produce a different variant of a structure it needs. For example, Vancomycin-resistant bacteria make a different cell wall compared to susceptible bacteria. The antibiotic is not able to interact as well with this type of cell wall.

Some bacteria are naturally resistant to certain antibiotics. Imagine for example an antibiotic that destroys the cell wall of the bacteria. If a bacterium does not have a cell wall, the antibiotic will have no effect. This phenomenon is called intrinsic resistance. When a bacterium that was previously susceptible to an antibiotic evolves resistance it is called acquired resistance.

Antibiotics are the main therapeutic tools to treat various bacterial infections. But today, more and more antibiotics are becoming less effective. It is because of the antibiotic resistance developed by bacteria due to the use and misuse of antibiotics. Antibiotic resistance is the acquired ability of a bacterium to resist the effects of an antibiotic to which it is normally susceptible. It occurs when bacteria change in a way that reduces the efficacy of antibiotics. Thus, the bacteria continue to multiply in the presence of therapeutic levels of antibiotics.

Resistant bacteria destroy the antibiotic or neutralize its effects. Antibiotic resistance is encoded by bacteria at either chromosome or plasmid.

Bacteria resistant to multiple antibiotics are called multidrug resistant (MDR) bacteria or superbugs.

Every living organism makes efforts to survive. If an organism adjusts itself to a changing environment, it survives, and if not, it dies. When bacteria constantly come in contact with antibiotics, some bacteria develop a resistance mechanism. Such bacteria have a greater chance of survival than those that are susceptible. Thus, antibiotic resistance is a natural phenomenon.