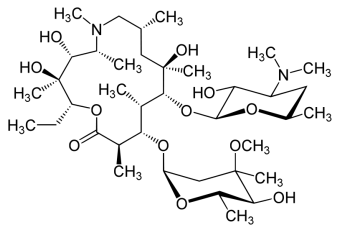
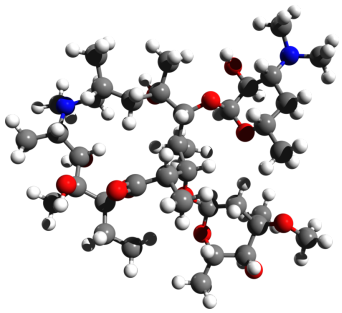
# Azithromycin

**Azithromycin**





| **Systematic (IUPAC) name** | |
|---|---|
| (2*R*,3*S*,4*R*,5*R*,8*R*,10*R*,11*R*,12*S*,13*S*,14*R*)-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-15-oxo-11-{[3,4,6-trideoxy-3-(dimethylamino)-β-D-*xylo*-hexopyranosyl]oxy}-1-oxa-6-azacyclopentadec-13-yl 2,6-dideoxy-3-*C*-methyl-3-*O*-methyl-α-L-*ribo*-hexopyranoside | |
| **Identifiers** | |
| **CAS number** | 83905-01-5 [1] |
| **ATC code** | J01 FA10 [2] S01 AA26 [3] |
| **PubChem** | CID 55185 [4] |
| **DrugBank** | APRD00397 [5] |
| **ChemSpider** | 10482163 [6] |
| **Chemical data** | |
| **Formula** | $C_{38}H_{72}N_2O_{12}$ |
| **Mol. mass** | 748.984 g·mol$^{-1}$ |
| **SMILES** | eMolecules [7] & PubChem [8] |
| **Synonyms** | 9-deoxy-9a-aza-9a-methyl-9a-homoerythromycin A |
| **Pharmacokinetic data** | |
| **Bioavailability** | 38% for 250 mg capsules |
| **Metabolism** | Hepatic |
| **Half-life** | 68 hours |
| **Excretion** | Biliary, renal (4.5%) |
| **Therapeutic considerations** | |
| **Pregnancy cat.** | B1(AU) B(US) |
| **Legal status** | |

| Routes | Oral (capsule or suspension), intravenous, ophthalmic |
|---|---|
| ✓ (what is this?) (verify) [9] | |

**Azithromycin** is an azalide, a subclass of macrolide antibiotics. Azithromycin is one of the world's best-selling antibiotics,[10] sold in the United States under the name **Zithromax**, and under a variety of brand names and generic labels worldwide. It is derived from erythromycin; however, it differs chemically from erythromycin in that a methyl-substituted nitrogen atom is incorporated into the lactone ring, thus making the lactone ring 15-membered.

Azithromycin is used to treat or prevent certain bacterial infections, most often those causing middle ear infections, tonsillitis, throat infections, laryngitis, bronchitis, pneumonia, Typhoid, and sinusitis. In recent years it has primarily been used to prevent bacterial infections in infants and those with weaker immune systems. It is also effective against certain venereal diseases, such as non-gonococcal urethritis, chlamydia, gonorrhea and cervicitis. Recent studies have also indicated it to be effective against late-onset asthma, but these findings are controversial and not widely accepted.[11] [12] Note that whereas the traditional zpack (500mg + 4 days of 250 mg) may be used in some instances, particularly for strep in pediatric cases, for adults over 88 pounds, the PDR calls for five (5) days of 500mg for strep throat, and yet the pediatric lesser dose is commonly mis-prescribed.[13]

## Etymology

Azithromycin's name is derived from the **az**ane-substituent and ery**thromycin**.

## History

A team of researchers at the Croatian pharmaceutical company Pliva, Gabrijela Kobrehel, Gorjana Radobolja-Lazarevski and Zrinka Tamburašev led by Dr. Slobodan Đokić, discovered azithromycin in 1980. It was patented in 1981, and was later found by Pfizer's scientists while going through patent documents. In 1986 Pliva and Pfizer signed a licensing agreement which gave Pfizer exclusive rights for the sale of azithromycin in Western Europe and the United States. Pliva brought their azithromycin on the market in Central and Eastern Europe under the brand name of Sumamed in 1988, Pfizer Zithromax in 1991, and Zentiva Azitrox. After several years, the U.S. Food and Drug Administration (FDA) approved AzaSite, an ophthalmic formulation of azithromycin, for the treatment of eye infections. AzaSite is currently marketed in the US by Inspire Pharmaceuticals.

## Available forms

Azithromycin is commonly administered in tablet or oral suspension (a one-dose version was made available in 2005). It is also available for intravenous injection and in a 1% ophthalmic solution. Tablets come in 250 mg and 500 mg doses. Oral suspension comes in 100 mg/5 mL and 200 mg/5 mL strengths. The 250 mg tablets are often dispensed in packages of six and commonly referred to as a "Z-Pak," whereas the 500 mg tablets are commonly available commercially in a pack of three tablets, or "Tri-Pak," intended as a three-day treatment. A common dose of oral azithromycin therapy consists of a "double dose" of medication on the first day of treatment and subsequent treatment for four or five additional days. With the "Z-Pak," this means two 250 mg tablets (a total of 500 mg) on the first day and one 250 mg tablet once daily for the next four days.

Pfizer brand-name (e.g., Zithromax) azithromycin tablets are mottled pink, unscored, film-coated, modified-oval-shaped tablets containing azithromycin monohydrate equivalent to 250 mg or 500 mg azithromycin and the following inactive ingredients: butylated hydroxytoluene, calcium phosphate, carmine, colloidal silicon dioxide, FD&C red # 40 lake, FD&C yellow # 6 lake, hypromellose (2910, 15cP), lactose monohydrate, magnesium stearate, pregelatinized starch, sodium lauryl sulfate, talc, titanium dioxide and triacetin. The 250 mg tablets have the following appearance: They are mottled pink, of a modified-oval-shape, and have "Pfizer" engraved into one side with "306" engraved into the other. The 500 mg tablet is similar in appearance with the exception of its relative size

and "ZTM500" engraved onto one side with "Pfizer" on the reverse. As with all medications, generic azithromycin tablets produced by companies other than Pfizer without the Zithromax brand name may have different appearances. For instance, the generic azithromycin sold under the Greenstone brand is pink, with the hexagonal "G" Greenstone, Ltd. logo engraved on one side and the numerals 3060 on the other. Greenstone, Ltd. is a subsidiary of Pfizer. The Novartis subsidiary Sandoz ships azithromycin as white oval tablets stamped with "GGD6" (250 mg) or "GGD8" (500 mg). A generic azithromycin made by Wockhardt is made as white oval tablets stamped with "W961" (250 mg).For this drug USP Reference standards are available(www.usp.org)

### Brand names

Azithromycin is sold under brand names APO-Azithromycin and Co Azithromycin in Canada; Zithromax in Finland, Italy, the United Kingdom, the United States, Australia, Portugal, South Africa, Canada, Thailand, Malaysia, Lebanon, Egypt and Belgium; Hemomicin in Serbia; Zithromac in Japan; Vinzam/Zitromax in Spain; Zmax; Sumamed in Bulgaria, Croatia, the Czech Republic, the Russian Federation, Slovakia and Slovenia; Azitrox in Czech Republic and Romania; Amixef in Peru; ATM, Aztrin, Azigard, Zitrocin, Azibiot, Azifine, AziCip, Azi Sandoz, Aziswift, AZORTA & AZEE, Azithral,Azibest, ZADY,Azistart,Vazir in India;[14] EZONEX of PharmaHealth, Azithrocin in Bangladesh, Tablets Winzith, zetro capsule and suspension; Saver (Laboratorios Elmer) in Venezuela; Azilide in India

Azithromycin 250 mg capsules ("zpack") from Ukraine

## Mechanism of action

Azithromycin prevents bacteria from growing by interfering with their protein synthesis. Azithromycin binds to the 50S subunit of the bacterial ribosome, and thus inhibits translation of mRNA. Nucleic acid synthesis is not affected.

## Microbiology

Azithromycin has a similar antimicrobial spectrum as erythromycin, but is more effective against certain Gram-negative bacteria, particularly *Haemophilus influenzae*. Azithromycin resistance has been described [15] and is endemic in many areas.

Azithromycin has been most effective against isolates of the following microorganisms:

- *Staphylococcus aureus*
- *Streptococcus agalactiae*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*
- *Haemophilus ducreyi*
- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- *Neisseria gonorrhoeae*
- *Chlamydia pneumoniae*
- *Chlamydia trachomatis*
- *Mycoplasma pneumoniae*
- *Helicobacter pylori*
- *Salmonella typhi*

- *Mycobacterium avium intracellulare*

It is notably ineffective against MRSA.

Azithromycin has been shown to be effective against malaria when used in combination with artesunate or quinine; the optimal dose for this is not yet known.[16]

## Pharmacokinetics

Unlike erythromycin, azithromycin is acid-stable and can therefore be taken orally with no need of protection from gastric acids. It is readily absorbed, but its absorption is greater on an empty stomach. Time to peak concentration in adults is 2.1 to 3.2 hours for oral dosage forms and 1 to 2 hours for intravenous (IV) forms. Due to the high concentration in phagocytes, azithromycin is actively transported to the site of infection. During active phagocytosis, large concentrations of azithromycin are released. The concentration of azithromycin in the tissues can be over 50 times higher than in plasma. This is due to ion trapping and the high lipid solubility.

Azithromycin's half-life allows a large single dose to be administered and yet maintain bacteriostatic levels in the infected tissue for several days. The new extended-release formulation of azithromycin "Zmax" is a liquid oral suspension that releases the drug in a single 2-g dose. With the macrolide technology of Zmax, this allows the drug to bypass the stomach, reducing gastrointestinal side effects of high-dose azithromycin.

## Metabolism

According to Davis' Drug Guide for Nurses, following a single 500 mg dose, the half-life of azithromycin is 11-14 hours. The longer half-life of 68 hours is achieved only when multiple doses are consumed, allowing a "steady state" of medication in the body.

Biliary excretion of azithromycin, predominantly unchanged, is a major route of elimination. Over the course of a week, approximately 6% of the administered dose appears as unchanged drug in urine.

## Side effects

Most common side effects are gastrointestinal; diarrhea (5%), nausea (3%), abdominal pain (3%) and vomiting. Fewer than 1% of patients stop taking the drug due to side effects. Nervousness, dermatologic reactions and anaphylaxis have been reported. As with all antimicrobial agents, pseudomembranous colitis can occur during and up to several weeks after azithromycin therapy. This drug may interfere with the effectiveness of birth control pills; other forms of contraception may be required during the treatment period. Azithromycin suspension has an objectionable taste, so can be difficult to administer to young children (i.e., 2-5 years), who may spit it out.

Occasional patients have developed cholestatic hepatitis or delirium. Accidental intravenous overdosage in an infant caused severe heart block, resulting in residual encephalopathy.[17] [18]

## External links

- Azithromycin - Yahoo! Health [19]
- MedicineNet.com - Azithromycin [20]
- Azithromycin (Zithromax) is a new-generation macrolide antibiotic - ABC of Mens Health [21]
- U.S. National Library of Medicine: Drug Information Portal - Azithromycin [22]

## References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[2] http://www.whocc.no/atc_ddd_index/?code=J01FA10

[3] http://www.whocc.no/atc_ddd_index/?code=S01AA26

[4] http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=55185

[5] http://www.drugbank.ca/cgi-bin/show_drug.cgi?CARD=APRD00397

[6] http://www.chemspider.com/Chemical-Structure.10482163

[7] http://www.emolecules.com/cgi-bin/search?t=ex&
q=CN%28C%29%5BC%40H%5D3C%5BC%40%40H%5D%28C%29O%5BC%40%40H%5D%28O%5BC%40%40H%5D2%5BC%40%40H%5D%28C%29%

[8] http://pubchem.ncbi.nlm.nih.gov/search/
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[9] http://en.wikipedia.org/w/index.php?&diff=cur&oldid=321837379

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[13] Physicians Desk Reference, Azithromycin, 2009.

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[18] R. Baselt, *Disposition of Toxic Drugs and Chemicals in Man*, 8th edition, Biomedical Publications, Foster City, CA, 2008, pp. 132-133.

[19] http://health.yahoo.com/caregiving-resources/azithromycin/healthwise--d00091a1.html

[20] http://www.medicinenet.com/azithromycin/article.htm

[21] http://www.abcmenshealth.com/24052009/azithromycin-zithromax-is-a-new-generation-macrolide-antibiotic.html

[22] http://druginfo.nlm.nih.gov/drugportal/dpdirect.jsp?name=Azithromycin

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