

Azithromycin (Zithromax) in Brief

- * **Active ingredient:** Azithromycin
- * **Common brand names:** Zithromax, Sumamed, Azasite, Z-pak
- * **Drug class:** Antibiotic, Macrolide, Azalide group
- * **Legal status:** Prescription only
- * **Pregnancy Category:** B
- * **Habit forming?** No
- * **Originally discovered:** 1981, Pliva, Croatia Croatia

Introduction

Azithromycin is the first macrolide antibiotic belonging to the azalide group. Azithromycin is derived from erythromycin by adding a nitrogen atom into the lactone ring of erythromycin A. Azithromycin is sold under the brand names Zithromax and Sumamed, and is one of the world's best-selling antibiotics.

History

Since the 1970s, PLIVA's (Croatian pharmaceutical company, based in Zagreb, Croatia) research team, led by Dr Slobodan Dokic, had been working in the area of macrolide antibiotics¹. In 1981, his team of researchers, Gabrijela Kobrehel, Zrinka Tamburasev and Gorjana Radobolja-Lazarevski, synthesised a novel antibiotic named azithromycin, the first member of a new class of macrolide antibiotics, termed azalides. Azithromycin dihydrate was obtained from the erythromycin molecule and demonstrated superior properties.

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, and Pfizer under the brand name Zithromax in 1991.

Because of its exceptional therapeutic properties, azithromycin revolutionised antibiotic treatment and became one of the most successful drugs worldwide. From its early trials, it proved to be an extremely efficient antibiotic with expanded and enhanced antibacterial activity (particularly against gram-negative pathogens), prolonged and higher tissue concentration and a low incidence of gastrointestinal side effects compared to other similar antibiotics.

FDA approved uses

Azithromycin is indicated for the treatment of the following infections due to susceptible strains of sensitive organisms:

- * Upper respiratory tract infections: pharyngitis/tonsillitis, sinusitis, otitis media
- * Lower respiratory tract infections: bronchitis, acute exacerbation of chronic bronchitis, community acquired pneumonia of mild severity.

* Sexually transmitted diseases: uncomplicated urethritis, uncomplicated cervicitis due to *Neisseria gonorrhoeae* or *Chlamydia trachomatis*.

* Chancroid (genital ulcer disease in men).

* Skin and soft tissue infections: erysipelas, impetigo, secondary pyoderma, erythema migrans.

* Mycobacterial Infections.

Off-label & Investigational uses

Off-label and investigational uses of Azithromycin include:

Infectious diseases:

* Pelvic inflammatory disease (PID)

PID comprises a spectrum of inflammatory disorders of the upper female genital tract, including any combination of endometritis, salpingitis, tubo-ovarian abscess, and pelvic peritonitis. Sexually transmitted organisms, *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are the major pathogens causing PID. Azithromycin provides a short simple treatment option for PID³.

* Infectious diarrhoea

Infectious diarrhoea is the most common cause of diarrhoea worldwide. Azithromycin is a good choice for pregnant women and children, for whom fluoroquinolones are not approved, and for patients who cannot otherwise tolerate fluoroquinolones⁴.

* Dental infections

Azithromycin is given to people allergic to penicillins and those who have abscesses and other dental infections, especially those extending into the sinuses, gums and bone, and for whom other antibiotics have proved ineffective.

* Acne

Acne vulgaris is a common inflammatory disorder of the skin. Oral antibiotics are known to be effective in its treatment. Azithromycin is a safe and effective alternative in the treatment of inflammatory acne with few side-effects.

A randomized study⁶ compared the efficacy of azithromycin with doxycycline. Facial lesions significantly improved with both drugs. Neither drug was shown to be more effective than the other. The beneficial effect continued until 2 months after treatment. This study indicates that azithromycin is at least as effective as doxycycline in the treatment of acne.

* Pertussis

Azithromycin is as effective as and better tolerated than erythromycin for the treatment of pertussis⁷.

* Prostatitis

Azithromycin is used in the treatment of chronic prostatitis caused by *Chlamydia trachomatis* and *Neisseria gonorrhoeae*.

* Syphilis

Azithromycin has been successfully used as a multidose treatment in persons who have early syphilis⁸.

* Mediterranean spotted fever (Rickettsiosis)

Mediterranean spotted fever, also known as boutonneuse fever, is transmitted by the dog tick *Rhipicephalus sanguineus* and has a characteristic rash and a distinct mark, a tache noire (black spot) at the site of the tick bite. Azithromycin is effective treatment in children and can be used as alternatives to doxycycline in adults⁹.

* Endocarditis

Azithromycin is used for prophylaxis of bacterial endocarditis in persons who are allergic to penicillin and undergoing surgical or dental procedures¹⁰.

Non-infectious diseases:

* Atherosclerosis

Azithromycin appears to reduce the risk of *Chlamydia pneumoniae*-induced atherosclerosis¹¹.

* Cystic fibrosis

According to the studies², azithromycin significantly improves quality of life, reduces the number of respiratory exacerbations, and reduces the rate of decline in lung function in persons with cystic fibrosis.

While the exact mechanisms are unknown, anti-inflammatory rather than antimicrobial properties of macrolides seem to be responsible for the beneficial effects.

Azithromycin "pros" and "cons"

Advantages:

- * Excellent efficacy. Many scientific studies have shown that azithromycin is better or equally effective compared to other antibiotics.

- * Low potential for drug interactions. Azithromycin, unlike the majority of macrolides, does not bind to cytochrome P-450 in the liver, resulting in low potential for drug to drug interaction.

- * Low rate of side effects. Side effects with azithromycin are mild to moderate, mostly gastrointestinal.

- * Sustained antimicrobial activity. Azithromycin reaches high and sustained tissue concentrations that results in sustained antimicrobial activity.

- * Active against intracellular bacteria (*Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Mycoplasma pneumoniae*, *Legionella* spp.). Since azithromycin is a weak base, it easily penetrates the cell membrane and stays within the cell.

- * Targeted activity at the site of infection. Because of the transport with white blood cells, azithromycin possesses a unique property - targeted activity at the site of infection. In infected tissues,

azithromycin achieves high and sustained therapeutic concentrations that last five to seven days after the last dose.

* Suitable choice for empirical therapy. Since azithromycin has a good activity against the most common pathogens it is used as a choice for empirical therapy.

* Good compliance: short once daily dosing regimen. Azithromycin's short dosing regimen is convenient and improves patient compliance. For the majority of infections, azithromycin is administered once daily for three days. In the treatment of sexually transmitted diseases, azithromycin is administered as a single dose.

* Active against most respiratory tract infections. Beta-lactams lack activity against atypical pathogens. Among macrolides, azithromycin shows the best activity against *H. influenzae*.

Disadvantages:

* Food reduces azithromycin absorption rate. Azithromycin capsules should not be mixed with or taken with food, however tablets may be taken without regard to food.

Mode of action

Azithromycin acts by interfering with bacterial protein synthesis. Although this mechanism is considered bacteriostatic, concentrations several times higher than minimum inhibitory concentrations (MIC) contribute to the bactericidal activity of azithromycin.

Non-antibiotic properties: immunomodulating effect

Data indicate that macrolides may have immunomodulatory activities: *in vitro* and *ex vivo* studies clearly show that macrolides can influence cytokine production by several cell types; furthermore, macrolides can alter polymorphonuclear cell functions *in vitro* and *ex vivo*. Although immunomodulation may serve as one explanation for the beneficial effects of macrolides in patients with chronic pulmonary inflammation, the effect of low-dose macrolide therapy on biofilm-formation may form a second explanation for the positive effects of long-term low-dose macrolide therapy.

Time for Azithromycin to clear out the system

The half-life of Azithromycin is about 68 hours. So it takes about 16-17 days to clear out of the system.

Azithromycin (Zithromax) for Chlamydia infection

Chlamydia trachomatis is the most common sexually transmitted infection worldwide, especially among adolescents and young adults. Chlamydia is a very guileful infection because many cases of infection are asymptomatic. Untreated infection can progress to persistent infection, which may initiate chronic diseases including pelvic inflammatory disease, ectopic pregnancy, tubal factor infertility, and chlamydia-induced arthritis, including Reiter's syndrome.

Chlamydia is sexually transmitted, usually through vaginal intercourse. Occasionally it is transmitted by oral sex or anal sex.

Azithromycin has revolutionized the treatment of chlamydial infections. Its importance comes from its highly favorable pharmacokinetic properties: acid stability, high tissue penetration, low serum levels and a very long half-life. Anti-chlamydial levels of the drug are readily achieved inside cells or tissues.

Adequate intracellular levels may be sustained for several days because of the slow efflux of the drug from cells.

According to the Centers for Disease Control and Prevention Guidelines azithromycin is a first-line treatment for chlamydial genital infections. Azithromycin is also recommended by the US Center for Disease Control and Prevention for the treatment of chlamydial genital tract infection in pregnant women

The recommended dose for the treatment of *Chlamydia trachomatis* is a single 1 gram (1000 mg) dose.

Recurrent Chlamydial infection

Relapsing (persistent) chlamydial infections are a common problem, even though patients are often treated appropriately. Azithromycin may be particularly effective against persistent chlamydial infection⁴.

Further reading

- * Azithromycin (Zithromax) versus Other Medications

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