

Azithromycin

Introduction: Azithromycin, an azalide, a subclass of macrolide antibiotics, for oral administration.

Mechanism of action: Azithromycin acts by binding to the 50S ribosomal subunit of susceptible microorganisms and, thus, interfering with microbial protein synthesis. Nucleic acid synthesis is not affected. Azithromycin concentrates in phagocytes and fibroblasts as demonstrated by *in vitro* incubation techniques. Using such methodology, the ratio of intracellular to extracellular concentration was >30 after one hour incubation. *In vivo* studies suggest that concentration in phagocytes may contribute to drug distribution to inflamed tissues.

Indications: Azithromycin is used to treat bacterial infections in many different parts of the body. It can be used to treat Streptococcal infections of the throat, Chlamydial infections, M.pneumoniae, C.jejuni, H.Influenzae, bronchitis, skin infections etc.

Dosage:

Infection*	Recommended Dose/Duration of Therapy
Community-acquired pneumonia (mild severity) Pharyngitis/tonsillitis (second line therapy) Skin/skin structure (uncomplicated)	500 mg as a single dose on Day 1, followed by 250 mg once daily on Days 2 through 5.
Acute bacterial exacerbations of chronic obstructive pulmonary disease (mild to moderate)	500 mg QD x 3 days OR 500 mg as a single dose on Day 1, followed by 250 mg once daily on Days 2 through 5.
Acute bacterial sinusitis	500 mg QD x 3 days
Genital ulcer disease (chancroid)	One single 1 gram dose
Non-gonococcal urethritis and cervicitis	One single 1 gram dose

Renal Insufficiency: No dosage adjustment is recommended for subjects with renal impairment (GFR \leq 80 mL/min). The mean AUC₀₋₁₂₀ was similar in subjects with GFR 10-80 mL/min compared to subjects with normal renal function, whereas it increased 35% in subjects with GFR $<$ 10 mL/min compared to subjects with normal renal function. Caution should be exercised when azithromycin is administered to subjects with severe renal impairment.

Hepatic Insufficiency: The pharmacokinetics of azithromycin in subjects with hepatic impairment have not been established. No dose adjustment recommendations can be made in patients with impaired hepatic function.

No dosage adjustment is recommended based on age or gender.

Pediatric Patients: Azithromycin for oral suspension can be taken with or without food.

Acute Otitis Media: The recommended dose of azithromycin for oral suspension for the treatment of pediatric patients with acute otitis media is 30 mg/kg given as a single dose or 10 mg/kg once daily for 3 days or 10 mg/kg as a single dose on the first day followed by 5 mg/kg/day on Days 2 through 5. (See chart below.)

Acute Bacterial Sinusitis: The recommended dose of azithromycin for oral suspension for the treatment of pediatric patients with acute bacterial sinusitis is 10 mg/kg once daily for 3 days. (See chart below.)

Community-Acquired Pneumonia: The recommended dose of azithromycin for oral suspension for the treatment of pediatric patients with community-acquired pneumonia is 10 mg/kg as a single dose on the first day followed by 5 mg/kg on Days 2 through 5. (See chart below.)

Side effects: Overall, the most common side effects in adult patients receiving a multiple-dose regimen of azithromycin were related to the gastrointestinal system with diarrhea/loose stools (5%), nausea (3%), and abdominal pain (3%) being the most frequently reported.

No other side effects occurred in patients on the multiple-dose regimen of azithromycin with a frequency greater than 1%. Side effects that occurred with a frequency of 1% or less included the following:

Cardiovascular: Palpitations, chestpain. **Gastrointestinal:** Dyspepsia, flatulence, vomiting, melena, and cholestatic jaundice. **Genitourinary:** Monilia, vaginitis, and nephritis. **Nervous System:** Dizziness, headache, vertigo, and somnolence. **General:** Fatigue. **Allergic:** Rash, photosensitivity, and angioedema.

Post-Marketing Experience: Adverse events reported with azithromycin during the post-marketing period in adult and/or pediatric patients for which a causal relationship may not be established include:

Allergic: Arthralgia, edema, urticaria, angioedema. **Cardiovascular:** Arrhythmias including ventricular tachycardia, hypotension. There have been rare reports of QT prolongation and *torsades de pointes*. **Gastrointestinal:** Anorexia, constipation, dyspepsia, flatulence, vomiting/diarrhea rarely resulting in dehydration, pseudomembranous colitis, pancreatitis, oral candidiasis and rare reports of tongue discoloration. **General:** Asthenia, paresthesia, fatigue, malaise and anaphylaxis (rarely fatal). **Genitourinary:** Interstitial nephritis and acute renal failure, vaginitis. **Hematopoietic:** Thrombocytopenia. **Liver/Biliary:** Abnormal liver function

including hepatitis and cholestatic jaundice, as well as rare cases of hepatic necrosis and hepatic failure, some of which have resulted in death.

Nervous System: Convulsions, dizziness/vertigo, headache, somnolence, hyperactivity, nervousness, agitation and syncope.

Psychiatric: Aggressive reaction and anxiety.

Skin/Appendages: Pruritus, rarely serious skin reactions including erythema multiforme, Stevens Johnson Syndrome, and toxic epidermal necrolysis.

Special Senses: Hearing disturbances including hearing loss, deafness, and/or tinnitus, rare reports of taste/smell perversion and/or loss.

Precautions: General: Because azithromycin is principally eliminated via the liver, caution should be exercised when azithromycin is administered to patients with impaired hepatic function. Due to the limited data in subjects with GFR<10 mL/min, caution should be exercised when prescribing azithromycin in these patients.

Pregnancy: No evidence of impaired fertility or harm to the fetus due to azithromycin was found. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, azithromycin should be used during pregnancy only if clearly needed.

Nursing Mothers :It is not known whether azithromycin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when azithromycin is administered to a nursing woman.

Pediatric Use: In controlled clinical studies, azithromycin has been administered to pediatric patients ranging in age from 6 months to 12 years. For information regarding the use of azithromycin in the treatment of pediatric patients.

Geriatric Use: Dosage adjustment does not appear to be necessary for older patients with normal renal and hepatic function receiving treatment with this dosage regimen.

Contraindications: Azithromycin is contraindicated in patients with known hypersensitivity to azithromycin, erythromycin, any macrolide or ketolide antibiotic.

How supplied: Customized as per request.