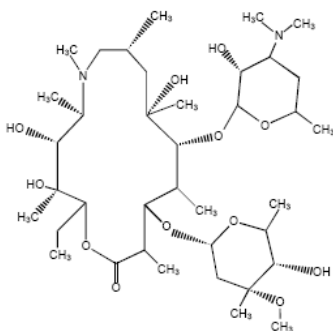


## **AZYXIN TABLETS / SUSPENSION**

### **Azithromycin**

#### **DESCRIPTION**

Azithromycin is an azalide, a subclass of macrolide antibiotics, for oral administration. Azithromycin is derived from erythromycin; however, it differs chemically from erythromycin in that a methyl-substituted nitrogen atom is incorporated into the lactone ring. Azithromycin has the following structural formula:



#### **COMPOSITION**

##### **AZYXIN-100 Suspension**

Each 5 ml contains:

Azithromycin IP equivalent to Azithromycin (anhydrous)	100 mg
Flavoured syrupy base	q.s.
Colour: Quinoline Yellow WS	

##### **AZYXIN-250/500 Tablet**

Each film coated tablet contains:

Azithromycin USP [as dihydrate]	
equivalent to Azithromycin anhydrous	250mg or 500mg

#### **CLINICAL PHARMACOLOGY**

Azithromycin acts by binding to the 50S ribosomal subunit of susceptible microorganisms, thus interfering with microbial protein synthesis.

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.

Azithromycin has been shown to be active against most isolates of the following microorganisms, both *in vitro* and in clinical infections.

#### **Aerobic and facultative gram-positive microorganisms**

*Staphylococcus aureus*  
*Streptococcus pneumoniae*  
*Streptococcus agalactiae*  
*Streptococcus pyogenes*

### **Aerobic and facultative gram-negative microorganisms**

*Haemophilus influenzae*  
*Moraxella catarrhalis*  
*Neisseria gonorrhoeae*  
*Haemophilus ducreyi*

### **"Other" microorganisms**

*Chlamydia pneumoniae*  
*Chlamydia trachomatis*  
*Mycoplasma pneumoniae*

N.B. Beta-lactamase production has no effect on azithromycin activity.

### **Pharmacokinetics**

- Azithromycin is more stable than erythromycin at gastric pH.
- The pharmacokinetic profile of azithromycin reflects a rapid and extensive uptake from the circulation into intracellular compartments, followed by slow release.
- Azithromycin levels in pulmonary macrophages, polymorphonuclear leukocytes, tonsillar tissue, and genital or pelvic tissue remain increased for extended periods, with a mean tissue half-life of 2 to 4 days. This feature allows single-dose therapy for STDs and 3- to 5-day regimens for skin, soft tissue, and some respiratory infections.

**Absorption:** The absolute bioavailability of Azithromycin 250 mg capsules is 38%.

**Distribution:** The serum protein binding of Azithromycin is variable depending upon the serum concentration, decreasing from 51% at 0.02 µg/mL to 7% at 2 µg/mL.

**Metabolism & Excretion:** Most of an absorbed dose of Azithromycin is eliminated unchanged, principally in the feces, and no metabolite is thought to have appreciable antimicrobial activity. Urinary excretion of the unchanged drug seems to be a minor elimination route, with less than 7% of a 500-mg dose recovered in the urine after 24 hours.

Terminal elimination half-life= 68 hours.

### **INDICATIONS**

**AZYXIN** (azithromycin) is indicated for the treatment of patients with mild to moderate infections caused by susceptible strains of the designated microorganisms in the specific conditions listed below.

#### **PEDIATRIC PATIENTS**

**Acute otitis media** caused by *Haemophilus influenzae*, *Moraxella catarrhalis* or *Streptococcus pneumoniae*.

**Pharyngitis/tonsillitis** caused by *Streptococcus pyogenes*.

**Community-acquired pneumonia** due to *Chlamydia pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae* or *Streptococcus pneumoniae* in patients appropriate for oral therapy.

#### **Skin and skin structure infections:**

Folliculitis, furuncles, carbuncles, impetigo, pyoderma, infected ulcer, infected dermatitis, cellulitis, and erysipelas due to *Staphylococcus aureus*, *S. pyogenes* or *S. agalactiae*.

**ADULTS**

**Acute bacterial exacerbations of chronic obstructive pulmonary disease** due to *Haemophilus influenzae*, *Moraxella catarrhalis* or *Streptococcus pneumoniae*.

**Acute bacterial sinusitis** due to *Haemophilus influenzae*, *Moraxella catarrhalis* or *Streptococcus pneumoniae*.

**Community-acquired pneumonia** due to *Chlamydia pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae* or *Streptococcus pneumoniae* in patients appropriate for oral therapy.

**Pharyngitis/tonsillitis** caused by *Streptococcus pyogenes*.

**Uncomplicated skin and skin structure infections** due to *Staphylococcus aureus*, *Streptococcus pyogenes*, or *Streptococcus agalactiae*. Abscesses usually require surgical drainage.

**Urethritis and cervicitis** due to *Chlamydia trachomatis* or *Neisseria gonorrhoeae*.

**Genital ulcer disease** in men due to *Haemophilus ducreyi* (chancroid).

**DOSAGE & ADMINISTRATION**

Food does not affect the absorption of azithromycin and it can be administered without regard to meals.

**PEDIATRIC PATIENTS**

**Acute Otitis Media:** The recommended dose of AZYXIN Suspension 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.

**Acute Bacterial Sinusitis:** The recommended dose of AZYXIN Suspension is 10 mg/kg once daily for 3 days.

**Community-Acquired Pneumonia:** The recommended dose of AZYXIN Suspension 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]

<b>OTITIS MEDIA &amp; COMMUNITY-ACQUIRED PNEUMONIA: (5-Day Regimen)</b>			
<b>Dosing Calculated on 10 mg/kg/day Day 1 and 5 mg/kg/day Days 2 to 5.</b>			
<b>Weight</b>		<b>100 mg/5 mL</b>	
<b>Kg</b>	<b>Lbs.</b>	<b>Day 1</b>	<b>Days 2-5</b>
5	11	2.5 ml (½ tsp)	1.25 ml (¼ tsp)
10	22	5 ml (1 tsp)	2.5 ml (½ tsp)

<b>OTITIS MEDIA &amp; ACUTE BACTERIAL SINUSITIS: (3-Day Regimen)</b>		
<b>Dosing Calculated on 10 mg/kg/day</b>		
<b>Weight</b>		<b>100 mg/5 mL</b>
<b>Kg</b>	<b>Lbs.</b>	<b>Day 1-3</b>
5	11	2.5 ml (½ tsp)
10	22	5 ml (1 tsp)

<b>OTITIS MEDIA: (1-Day Regimen)</b>		
<b>Dosing Calculated on 30 mg/kg as a single dose</b>		
<b>Weight</b>		<b>100 mg/5 mL</b>
<b>Kg</b>	<b>Lbs.</b>	<b>Day 1</b>
5	11	7.5 ml (1½ tsp)
10	22	15 ml (3 tsp)
20	44	30ml (6 tsp)

## ADULTS

Infection	Recommended Dosage & Duration Of Therapy
<b>CAP [mild] Pharyngitis/Tonsillitis Skin/Skin Structure (uncomplicated)</b>	Day 1: 500mg as a single dose Day 2-5: 250mg once daily
<b>Acute Bacterial Exacerbations of Chronic Obstructive Pulmonary Disease</b>	500mg QD x 3 days <b>or</b> Day 1: 500mg as a single dose Day 2-5: 250mg once daily
<b>Acute Bacterial Sinusitis</b>	500mg QD x 3 days
<b>Genital Ulcer Disease (chancroid)</b>	One single 1 gram dose
<b>Non-gonococcal Urethritis &amp; Cervicitis</b>	One single 1 gram dose
<b>Gonococcal Urethritis &amp; Cervicitis</b>	One single 2 gram dose

### Renal Insufficiency

No dosage adjustment is recommended for subjects with renal impairment (GFR  $\leq$  80 mL/min). 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.

### CONTRAINDICATIONS

**Azyxin** Suspension/Tablets are contraindicated in patients with known hypersensitivity to Azithromycin, any macrolide or ketolide antibiotic.

### WARNINGS

Rare serious allergic reactions have been reported rarely in patients on azithromycin therapy. If an allergic reaction occurs, the drug should be discontinued and appropriate therapy instituted.

Pseudomembranous colitis has been reported with nearly all antibacterial agents and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Mild cases of pseudomembranous colitis usually respond to discontinuation of the drug alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis.

### 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

Prolonged cardiac repolarization and QT interval, imparting a risk of developing cardiac arrhythmia and *torsades de pointes*, have been seen in treatment with other macrolides. A similar effect with azithromycin cannot be completely ruled out in patients at increased risk for prolonged cardiac repolarization.

### **Pregnancy**

**Pregnancy Category B:** There are, no adequate and well-controlled studies in pregnant women. Therefore 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.

### **DRUG INTERACTIONS**

Human clinical and pharmacokinetic studies have shown no major drug-drug interactions between azithromycin and numerous other agents: carbamazepine, theophylline, midazolam, terfenadine, cetirizine, atorvastatin, Trimethoprim/Sulfamethoxazole, sildenafil, zidovudine, fluconazole or cimetidine. The extent of absorption of azithromycin was unaffected by concurrent administration of antacids.

### **ADVERSE EFFECTS**

**Allergic:** Rash, pruritus, photosensitivity and angioedema.

**Cardiovascular:** Arrhythmias including ventricular tachycardia and hypotension. There have been rare reports of QT prolongation and *torsades de pointes*.

**Gastrointestinal:** Anorexia, constipation, dyspepsia, flatulence, vomiting/diarrhea.

**Genitourinary:** Interstitial nephritis, vaginitis.

**Nervous System:** dizziness/vertigo, headache, somnolence, nervousness, agitation.

**General:** Asthenia, paresthesia, fatigue, malaise.

### **PRESENTATION**

**AZYXIN Suspension** is available in bottles of 15 ml

**AZYXIN-250 Tablets** is available in blister strips of 6

**AZYXIN-500 Tablets** is available in blister strips of 3