

## **AZYXIN PLUS**

### **(Azithromycin plus Ambroxol Tablets)**

#### **DESCRIPTION**

**Azithromycin** is an azalide antibiotic, a subclass of the macrolides. The antibiotic is commonly used for treating respiratory tract infections.

**Ambroxol** is a mucolytic agent used in the treatment of respiratory diseases associated with viscid or excessive mucus.

#### **COMPOSITION**

Each film coated bilayered tablet of **Azyxin Plus 250mg** contains:

Azithromycin IP equivalent to Azithromycin (anhydrous)	250 mg
Ambroxol Hydrochloride [in sustained release form]	75 mg

Each film coated bilayered tablet of **Azyxin Plus 500mg** contains:

Azithromycin IP equivalent to Azithromycin (anhydrous)	500 mg
Ambroxol Hydrochloride [in sustained release form]	75 mg

#### **CLINICAL PHARMACOLOGY**

Ambroxol is a mucolytic agent and an active metabolite of bromhexine. Ambroxol acts to reduce the viscosity of tenacious mucus secretions by fragmentation of long mucopolysaccharide chains. This results in a productive cough which aids expectoration of liquefied mucoid respiratory secretions, and assists in clearing and maintaining patent bronchioles and alveoli. Ambroxol enhances the concentrations of antibiotics in pulmonary tissue thereby ensuring a more rapid recovery.

Azithromycin retains the spectrum of activity of erythromycin against Gram-positive pathogens but has increased activity against Gram-negative and atypical microorganisms. Azithromycin prevents bacteria from growing by interfering with their protein synthesis. It binds to the 50S subunit of the bacterial ribosome, and inhibits translation of mRNA. Nucleic acid synthesis is not affected.

Azithromycin concentrates in phagocytes and fibroblasts as demonstrated by *in vitro* incubation techniques. The ratio of intracellular to extracellular concentration is >30 after one hour incubation. *In vivo* studies suggest that concentration in phagocytes may contribute to drug distribution to inflamed tissues.

#### **Microbiology**

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

##### **Aerobic Gram-Positive Microorganisms**

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

##### **Aerobic Gram-Negative Microorganisms**

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

### "Other" Microorganisms

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

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

### INDICATIONS

**Azyxin Plus** 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.

- Upper Respiratory Tract Infections
  - Pharyngitis/Tonsillitis
  - Acute Bacterial Sinusitis
  - Otitis Media
- Lower Respiratory Tract Infections
  - Acute Bacterial Exacerbations Of Chronic Obstructive Pulmonary Disease
  - Community-Acquired Pneumonia [CAP]

### DOSAGE & ADMINISTRATION

#### ADULTS:

INFECTION	Recommended Dosage & Duration Of Therapy
CAP [mild] Pharyngitis/Tonsillitis	Day 1: 500mg as a single dose Day 2-5: 250mg once daily
Acute bacterial exacerbations of Chronic Obstructive Pulmonary Disease	500mg QD x 3 days or Day 1: 500mg as a single dose Day 2-5: 250mg once daily
Acute bacterial sinusitis	500mg QD x 3 days

N.B. **Azyxin Plus** Tablet should be swallowed whole and not chewed, crushed or divided. Azithromycin tablets may be taken without regard to food.

### Renal Insufficiency

No dosage adjustment is recommended for subjects with mild-moderate renal impairment (GFR $\leq$ 80mL/min). The mean AUC 0–120 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 $<$ 10mL/min compared to subjects with normal renal function. Caution should be exercised when azithromycin is administered to subjects with severe renal impairment.

### CONTRAINDICATIONS

**Azithromycin Plus** is contraindicated in patients with known hypersensitivity to ambroxol, azithromycin, erythromycin, or any macrolide antibiotic.

### PRECAUTIONS

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 should be instituted.

Pseudomembranous colitis has been reported with nearly all antibacterial agents. Therefore, it is important to consider this diagnosis in patients who present with

diarrhea subsequent to their administration. Mild cases usually respond to discontinuation of the drug alone. In moderate to severe cases, patients may have to be administered fluids and electrolytes, protein supplements and an antibacterial drug clinically effective against *Clostridium difficile* colitis.

Because azithromycin is principally eliminated via the liver, caution should be exercised when azithromycin is administered to patients with severe 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.

Ambroxol is required to be administered with caution in those with peptic ulceration, severe hepatic and renal dysfunction.

### **Pregnancy**

There are no adequate and well-controlled studies in pregnant women. Therefore Azyxin Plus should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

### **Nursing Mothers**

It is not known whether **Azyxin Plus** is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when **Azyxin Plus** is administered to a nursing woman.

### **DRUG INTERACTIONS**

**Azithromycin:** Human clinical and pharmacokinetic studies have shown no major drug-drug interactions between azithromycin and numerous other agents: 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.

**Ambroxol:** No specific drug interactions noted.

### **ADVERSE REACTIONS**

In clinical trials, most of the reported side effects with azithromycin were mild to moderate in severity and were related to the gastrointestinal tract, e.g., nausea, vomiting, diarrhea, or abdominal pain. Rarely but potentially serious side effects were angioedema and cholestatic jaundice.

**Ambroxol:** The side effects on account of ambroxol include gastrointestinal side effects, skin rashes, headache, dizziness and sweating.

### **PRESENTATION**

**Azyxin Plus 250mg/500mg** is available in blister strips of 3 tablets