For the use only of Registered Medical Practitioner

1. Generic Name and Brand Name

Azithromycin Tablets I.P. 500 mg
Azitough® – 500

Azithromycin Tablets I.P. 250 mg
Azitough ® - 250

2. Qualitative and Quantitative Composition:

Azitough – 500
Each film coated tablet contains:
Azithromycin Dihydrate I.P.
Eq. to Azithromycin Anhydrous ……500 mg
Excipients q.s.
Colour: Titanium Dioxide I.P.

Azitough – 250
Each film coated tablet contains:
Azithromycin Dihydrate I.P.
Eq. to Azithromycin Anhydrous ……..250 mg
Excipients q.s.
Colour: Titanium Dioxide I.P.

3. Dosage Form & strength

Refer section 1 & 2

4. Clinical particulars

4.1 Therapeutic indication

In the treatment of mild to moderate susceptible infection including R.T.I., uncomplicated skin / skin structure, non-gonococcal urethritis cervicitis. For susceptible infections including community acquired pneumonia, pelvic inflammatory diseases.

4.2 Posology and method of administration

Posology

Azitough can be taken with or without food.

Adults

Infection	Recommended dose, frequency and duration
Respiratory tract infection	500 mg once daily for 3 days OR 500 mg as a single dose on Day 1, followed by 250 mg once daily on Days 2 through 5
Uncomplicated skin /skin structure	
Community acquired pneumonia	
Non-gonoccoal urethritis cervicitis	One single 1 gram dose

Children

Infection	Recommended dose, frequency and duration
Community acquired pneumonia	10 mg/kg as a single dose on Day 1 followed by 5 mg/kg once daily on Days 2 through 5.
Respiratory tract infection	10 mg/kg once daily for 3 days. OR 12 mg/kg once daily for 5 days.

Method of Administration:

4.3 Contraindications

- Contraindicated in patients with a known hypersensitivity to azithromycin, erythromycin, any macrolide or ketolide drug.
- Contraindicated in patients with a history of cholestatic jaundice/hepatic dysfunction associated with prior use of azithromycin.

4.4 Special warnings and precautions for use

Hypersensitivity:

Serious allergic reactions, including angioedema, anaphylaxis, fatalities and dermatologic reactions including Stevens-Johnson syndrome, Acute generalized Exanthematosus Pustulosis (AGEP) and toxic epidermal necrolysis have been reported in patients on azithromycin therapy.

Despite initially successful symptomatic treatment of the allergic symptoms, when symptomatic therapy was discontinued, the allergic symptoms recurred soon there after in some patients without further azithromycin exposure. These patients required prolonged periods of observation and symptomatic treatment. The relationship of these episodes to the long tissue half-life of azithromycin and subsequent prolonged exposure to antigen is presently unknown.

If an allergic reaction occurs, the drug should be discontinued and appropriate therapy should be instituted. Physicians should be aware that allergic symptoms may reappear when symptomatic therapy has been discontinued.

Hepatotoxicity

Abnormal liver function, hepatic necrosis, hepatitis, cholestatic jaundice, and hepatic failure have been reported, some of which have resulted in death. Discontinue azithromycin immediately if signs and symptoms of hepatitis occur.

QT Prolongation

Prolonged cardiac repolarization and QT interval, imparting a risk of developing cardiac arrhythmia andtorsades de pointes, have been seen with treatment with macrolides, including azithromycin.

Providers should consider the risk of QT prolongation which can be fatal when weighing the risks and benefits of azithromycin for at-risk groups including: patients with known prolongation of the QT interval, congenital long QT syndrome, bradyarrhythmias or uncompensated heart failure

patients, a history of torsades de pointes, on drugs known to prolong the QT interval patients with ongoing proarrhythmic conditions such as uncorrected hypokalemia or hypomagnesemia, clinically significant bradycardia, and in patients receiving Class IA (quinidine, procainamide) or Class III (dofetilide, amiodarone, sotalol) antiarrhythmic agents. Elderly patients may be more susceptible to drug-associated effects on the QT interval.

Clostridium difficile-Associated Diarrhea (CDAD)
Clostridium difficile-associated diarrhea in severity from mild diarrhea to fatal colitis has been reported with use of nearly all antibacterial agents including azithromycin. Treatment with antibacterial agents alters the normal flora of the colon, leading to overgrowth of C. difficile.
C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antibacterial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

Exacerbation of myasthenia gravis
Exacerbation of symptoms of myasthenia gravis and new onset of myasthenic syndrome has been reported in patients receiving azithromycin therapy.

Use in Sexually Transmitted Infections
Azithromycin, at the recommended dose, should not be relied upon to treat syphilis. Antibacterial agents used to treat non-gonococcal urethritis may mask or delay the symptoms of incubating syphilis. All patients with sexually transmitted urethritis or cervicitis should have a serologic test for syphilis and appropriate testing for gonorrhea performed at the time of diagnosis. Appropriate antibacterial therapy and follow-up tests for these diseases should be initiated if infection is confirmed.

Development of Drug-Resistant Bacteria
Prescribing Azithromycin in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Mutagenesis
Azithromycin does not have a mutagenic potential.

Pregnancy
Pregnancy Category B. Azithromycin should be used during pregnancy only if clearly needed.

Lactation
Azithromycin is excreted in human milk in small amount. Caution should be exercised when azithromycin is administered to a nursing woman.

Pediatric Use:
Safety and effectiveness in the treatment of pediatric patients with acute bacterial sinusitis and community-acquired pneumonia under 6 months of age have not been established. Safety and effectiveness in the treatment of pediatric patients with pharyngitis/tonsillitis under 2 years of age have not been established.

Geriatric Use:
Elderly patients may be more susceptible to development of torsades de pointes arrhythmias than younger patients.

4.5 Drug Interactions
The important drug interactions are listed below

No	Drug	Drug interaction	**Remark**
1	Nelfinavir	adverse reactions of azithromycin, such as liver enzyme abnormalities and hearing impairment,	Close monitoring recommended.
2	Warfarin	may increase coagulation times	Monitor prothrombin time

4.6 Use in special populations (Pregnancy, Nursing woman, Pediatric use, Geriatric use)
Pregnancy : Category B

In the animal studies, no evidence of 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.

Lactation
Azithromycin has been reported to be excreted in human breast milk in small amounts. Caution should be exercised when azithromycin is administered to a nursing woman.

Pediatric Use
Safety and effectiveness in the treatment of pediatric patients with acute otitis media, acute bacterial sinusitis and community-acquired pneumonia under 6 months of age have not been established.
Use of azitrhomycin for the treatment of acute bacterial sinusitis and community-acquired pneumonia in pediatric patients (6 months of age or greater) is supported by adequate and well-controlled trials in adults

Pharyngitis/Tonsillitis: Safety and effectiveness in the treatment of pediatric patients with pharyngitis/tonsillitis under 2 years of age have not been established.

Geriatric Use
No overall differences in safety or effectiveness were observed between geriatric patients subjects and younger but greater sensitivity of some older individuals cannot be ruled out. Elderly patients may be more susceptible to development of torsades de pointes arrhythmias than younger patients.

4.7 Effects on ability to drive and use machines
There is no evidence to suggest that azithromycin may have an effect: on a patient's ability to drive or operate machinery. Visual impairment and vision blurred may have an effect on a patient's ability to drive or operate machinery

4.8 Undesirable effects
Cardiovascular: Palpitations, chest pain, Arrhythmias including ventricular tachycardia and hypotension, reports of QT prolongation and torsades de pointes.
Gastrointestinal: Dyspepsia, flatulence, vomiting, melena, cholestatic jaundice, diarrhea, loose stools, nausea, abdominal pain, constipation, anorexia, enteritis, flatulence, gastritis, jaundice, loose stools, pseudomembranous colitis, pancreatitis, oral candidiasis, pyloric stenosis, tongue discoloration and oral moniliasis.
Hematologic and Lymphatic: Thrombocytopenia, anemia and leukopenia.
Liver/Biliary: Abnormal liver function, hepatitis, cholestatic jaundice, hepatic necrosis, and hepatic failure.
Genitourinary: Monilia, vaginitis, and nephritis.
Nervous System: Dizziness, headache, vertigo, and somnolence, otitis media, hyperkinesia, agitation, nervousness, and insomnia.
General: Fatigue, Fever, face edema, fatigue, fungal infection, malaise, and pain.
Respiratory: Cough, pharyngitis, pleural effusion, rhinitis.
Skin and Appendages: Eczema, fungal dermatitis, pruritus, sweating, urticaria, and vesiculobullous rash.
Special Senses: Conjunctivitis.
Allergic: Rash, pruritus, photosensitivity, arthralgia, edema, urticaria, angioedema, allergic reaction and Azithromycin induced acute generalized exanthematous pustulosis (AGEP).

4.9 Overdose
Adverse reactions experienced at higher than recommended doses were similar to those seen at normal doses particularly nausea, diarrhea, and vomiting.
In the event of overdosage, general symptomatic and supportive measures are indicated as required.

5. Pharmacological properties
5.1 Mechanism of action
Azithromycin acts by binding to the 23S rRNA of the 50S ribosomal subunit of susceptible microorganisms inhibiting bacterial protein synthesis and impeding the assembly of the 50S ribosomal subunit.

5.2 Pharmacodynamic Properties

Azithromycin is a macrolide antibacterial drug.It acts by binding to the 50S ribosomal subunit of susceptible microorganisms and interferes with bacterial protein synthesis. Nucleic acid synthesis is not affected.

Cross Resistance

Azithromycin demonstrates cross resistance with erythromycin resistant Gram positive isolates.
Azithromycin has been shown to be active against most isolates of the following bacteria, both in vitro and in clinical:

Gram-Positive Bacteria

Staphylococcus aureus
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes

Gram-Negative Bacteria

Haemophilus ducreyi
Haemophilus influenzae
Moraxella catarrhalis
Neisseria gonorrhoeae

Other Bacteria

Chlamydophila pneumoniae
Chlamydia trachomatis
Mycoplasma pneumoniae

5.3 Pharmacokinetic properties

Absorption	Food was shown to increase Cmax by 23% but had no effect on AUC.
Distribution	Serum protein binding of azithromycin is variable in the concentration range approximately decreasing from 51%at 0.02 µg/mL to 7% at 2 µg/mL.
Excretion	Plasma concentrations of azithromycin following single 500 mg oral and IV doses declined in apolyphasic pattern resulting in a mean apparent plasma clearance of 630 mL/min and terminal elimination half-life of 68 hours.
Half life	Terminal elimination half-life of 68 hours.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have not been performed to evaluate carcinogenic potential. Azithromycin has shown no mutagenic potential in standard laboratory tests: mouse lymphoma assay, human lymphocyte clastogenic assay, and mouse bone marrow clastogenic assay. No evidence of impaired fertility due to azithromycin was found in rats given daily doses up to 10 mg/kg (approximately 0.2 times an adult daily dose of 500 mg based on body surface area).

Animal Toxicology and/or Pharmacology
Phospholipidosis (intracellular phospholipid accumulation) has been observed in some tissues of mice, rats, and dogs given multiple doses of azithromycin. Phospholipidosis has been observed in neonatal dogs (10 mg/kg/day) at maximum mean whole blood concentrations of 3.54 mcg/mL, approximately 3 times the pediatric dose Cmax. The significance of these findings for animals and for humans is unknown.

7. Description
Azitough 250 is supplied for oral administration, as a film coated tablet of Azithromycin. Each film coated tablet of Azitough 250 Azithromycin Dihydrate Eq. to Azithromycin Anhydrous 250 mg.

Azitough 500 is supplied for oral administration, as a film coated tablet of Azithromycin. Each film coated tablet of Azitough 500 Azithromycin Dihydrate Eq. to Azithromycin Anhydrous 500 mg.

8. Pharmaceutical particulars
8.1 Incompatibilities
Not Applicable

8.2 Shelf Life
Refer Pack

8.3 Packaging Information
Refer Pack

8.4 Storage condition
Refer Pack

9. Patient Counseling Information
Azithromycin tablets can be taken with or without food.
Patients should also be cautioned not to take aluminum-and magnesium-containing antacids and azithromycin simultaneously.

The patient should be directed to discontinue azithromycin immediately and contact a physician if any signs of an allergic reaction occur.

Direct parents or caregivers to contact their physician if vomiting and irritability with feeding occurs in the infant.

Patients should be counseled that antibacterial drugs including azithromycin should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When azithromycin is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of the therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the

effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by azithromycin or other antibacterial drugs in the future.

Diarrhea is a common problem caused by antibacterials which usually ends when the antibacterial is discontinued. Sometimes after starting treatment with antibacterials patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibacterial drug. If this occurs, patients should contact their physician as soon as possible.

10. Details of manufacturer
Refer Pack for manufacturer details.

Marketed by:
Abbott Healthcare Pvt. Ltd.
Angel Space, Bldg. D-4, Gala No. 1 to 3 & 11 to 13
Ground Floor, 101 to 106 & 111 to 116 First Floor,
201 to 206 & 211 to 216 2nd Floor, Pimplas,
Dist. Thane, Bhiwandi - 421 302, Maharashtra, India.

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11. Details of permission or licence number with date
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12. Date of revision
Version: 1.0, Dated: 18th Nov 2024

For Product Complaints/Adverse events or Queries please write to
webmasterindia@abbott.com