Azomyne®
Azithromycin

Properties:
Azomyne® (Azithromycin) is an azalide, a sub class of macrolide antibiotics, for oral administration. It acts by binding to the 50S ribosomal subunit of susceptible organisms and thus interfering with microbial protein synthesis. Azomyne® is rapidly absorbed and widely distributed throughout the body. Due to its high tissue affinity, the tissue concentrations exceed those in plasma up to 50 times and the tissue half-lives range between 2 and 4 days. Therefore, the dosage regimen for Azomyne® differs from that of other antimicrobials.

Antimicrobial activity:
Azomyne® is active against the following microorganisms:

- **Gram-positive aerobic bacteria**: *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, alpha-haemolytic streptococci (viridans group) and other *streptococci*, and *Corynebacterium diptheriae*.
  
  Because of an existing cross-resistance to erythromycin-resistant gram-positive strains and most strains of methicillin-resistant staphylococci, azithromycin should not be used in these cases.

- **Gram-negative aerobic bacteria**: *Haemophilus influenzae* and *parainfluenzae*, *Moraxella catarrhalis*, *Acinetobacter species*, *Yersinia species*, *Legionella pneumophila*, *Bordetella pertussis* and *parapertussis*, *Plesiomonas shigelloides*, *Pasteurella* species and *Vibrio cholerae* and *parahaemolyticus*. Activity against *Escherichia coli*, *Salmonella enteritidis* and *typhi*, *Enterobacter species*, *Aeromonas hydrophila*, and *Klebsiella species* is variable, therefore, susceptibility testing should be performed.

- **Anaerobic bacteria**: *Bacteroides fragilis* and *Bacteroides* species, *Clostridium perfringens*, *Peptococcus* and *Peptostreptococcus* species, *Fusobacterium necrophorum* and *Propionibacterium acnes*.

- **Micro-organisms causing sexually transmitted diseases**: *Chlamydia trachomatis*, *Treponema pallidum*, *Neisseria gonorrhoea*, and *Haemophilus ducreyi*.

- **Other micro-organisms**: *Borrelia burgdorferi*, *Chlamydia pneumoniae*, *Toxoplasma gondii*, *Mycoplasma pneumoniae* and *hominis*, *Ureaplasma urealyticum*, *Pneumocystis carinii*, *Mycobacterium avium*, *Campylobacter species* and *Listeria monocytogenes*.

Indications:
Azomyne® is indicated for the treatment of:

- Upper respiratory tract infections including: Sinusitis, pharyngitis and tonsillitis. (Azithromycin is not the drug of first choice for the treatment of tonsillitis or pharyngitis due to streptococci or for the prophylaxis of rheumatic fever. So far, there are no epidemiologic long-term studies of the efficacy of such a prophylaxis or for the frequency of possible late sequelae after 5-day therapy).

- Lower respiratory tract infections including: Bronchitis and pneumonia.

- Otitis media.

- Skin and soft tissues infections.

- Sexually transmitted diseases caused by *Chlamydia trachomatis* or *Neisseria gonorrhoea* (non multi-resistant stains); concurrent use in *Treponema pallidum* should be excluded.

Dosage and administration:

- **Azomyne®** is given as a once daily dose at least 1 hour before or 2 hours after food.

  **Adults and children weighing 45 kg or more:**

  - Sexually transmitted diseases: 1 g azithromycin once, i.e., 4 capsules once.
  - All other indications: The total dose is 1.5 g of azithromycin given as: 3-day or 5-day regimen:
    - 3-day therapy: 500 mg of azithromycin daily, i.e., 2 capsules once daily for three days.
    - Alternative 5-day therapy: 500 mg of azithromycin as a single dose on day 1, i.e., 2 capsules, followed by 250 mg azithromycin, i.e., 1 capsule on days 2-5.
  
  The efficacy of a 5-day regimen of azithromycin in the treatment of patients with pneumonia is sufficient in most cases.

- **Children weighing less than 45 kg**: 10 mg/kg as a single dose for 3 consecutive days.

  - No dosage adjustment is required in patients with impaired renal function up to a creatinine of ≥ 40 ml/min.
Contraindications:
- Hypersensitivity to azithromycin or macrolide antibiotics such as erythromycin.
- Severe hepatic diseases, as it is mainly excreted via the liver.

Drug interactions:
- Mineral antacids: Azithromycin and mineral antacids should not be taken simultaneously, since mineral antacids reduce the peak plasma level of azithromycin (without affecting the extent of absorption). Therefore, a time interval of 2-3 hours should be observed.
- Cimetidine: Has no influence on azithromycin absorption; therefore, it can be co-administered with azithromycin.
- Ergot Alkaloids: Although no experience is available so far, vasoconstricting effects with circulatory disorders in particular of fingers and toes cannot be excluded if azithromycin and dihydroergotamine or non-hydrated ergot alkaloids are administered concomitantly. Therefore, concomitant administration should be avoided for safety reasons.
- Theophylline: Clinical studies have not revealed any evidence of interaction between azithromycin and theophylline. Since interactions between theophylline and some macrolides have been reported, careful monitoring of patients taking theophylline and azithromycin concomitantly is advised.
- Macrolide-antibiotics are known to interact with triazolam, cyclosporin, and digoxin. For azithromycin, sufficient data are not available but the possibility of interactions should be borne in mind.
- In healthy subjects studies, co-administration of azithromycin did not significantly affect carbamazepine or its active metabolite levels or methylprednisolone.
- Other antibiotics: For the potential of parallel resistance between azithromycin and macrolide antibiotics (e.g., erythromycin) as well as lincomycin and clindamycin, co-administration of azithromycin with these drugs is not recommended.

Warnings:
- Hypersensitivity reactions are rare during azithromycin treatment. They include reddening of the skin and mucosa with or without pruritus. As with erythromycin and other macrolides, severe allergic reactions including reversible local swellings of skin, angioedema and anaphylaxis have been reported in rare cases during azithromycin treatment.
- In patients with severe and persistent diarrhoea, the possibility of life-threatening pseudomembranous colitis should be borne in mind. In such cases, azithromycin treatment should be immediately terminated and appropriate therapy instituted.
- In high dose preclinical studies, azithromycin has been noted to cause reversible phospholipidosis. There is no evidence that this is of relevance to the normal use of azithromycin in humans.
- As with any antibiotic, observation for signs of superinfection with non-susceptible organisms including fungi is recommended and appropriate therapy should be instituted, if necessary.
- Prolonged cardiac repolarisation and QT interval, imparting a risk of developing cardiac arrhythmia and torsades de pointes, have been seen in treatment with macrolides, therefore caution is required when treating patients:
  • With congenital or documented QT prolongation.
  • Currently receiving treatment with other active substance known to prolong QT interval such as antiarrhythmics of classes la and III, cisapride and terfenadine.
  • With electrolyte disturbance, particularly in case of hypokalaemia and hypomagnesemia.
  • With clinically relevant bradycardia, cardiac arrhythmia or severe cardiac insufficiency.

Precautions:
- Caution should be exercised when using azithromycin in patients with severe renal insufficiency (creatinine clearance < 40 ml/min).
- Pregnancy: Category B; there are no adequate and well controlled studies in pregnant women; use during pregnancy only if clearly needed.
- **Lactation**: It is not known whether azithromycin is excreted in breast milk. Because many drugs are excreted in human milk, caution should be exercised when azithromycin is administered to a nursing woman.

**Undesirable effects:**
- Gastrointestinal tract: Diarrhoea, abdominal pain, spasms, nausea, vomiting and flatulence may occasionally occur.
- Hepatobiliary system: Reversible increase in liver enzymes (transaminases, alkaline phosphatase) and in serum bilirubin were rarely observed.
- Blood and blood corpuscles: Blood count changes (neutropenia) were observed in individual cases.

**Overdosage:**
Data on overdosage are not available. When overdosage occurs, gastric lavage and general supportive measures are indicated.

**Information for the patient:**
- Take **Azomyne®** at least 1 hour before meals or 2 hours after meals.
- Do not take **Azomyne®** with antacids containing aluminum or magnesium.
- Swallow the whole capsule with adequate amount of liquid.
- Discard unused suspension after 5 days of reconstitution.

**Pharmaceutical particulars:**

**Shelf life:**
2 years

**Storage conditions:**
Store below to 30°C.

**Presentations:**
- **Azomyne®** Capsules: Each capsule contains 250 mg Azithromycin (dihydrate) in packs of 6 capsules.
- **Azomyne®** Dry Suspension (15 ml): Each 5 ml contains 200 mg Azithromycin (dihydrate) in bottles of 15 ml after reconstitution.
- **Azomyne®** Dry Suspension (22.5 ml): Each 7.5 ml contains 300 mg Azithromycin (dihydrate) in bottles of 22.5 ml after reconstitution.

* Some presentations may not be available in certain countries

(This is a medicament - keep medicaments out of the reach of children)

- Medicament is a product that affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor’s prescription, the method of use and the instructions of the pharmacist who dispensed the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

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