Summary of Product Characteristics
AZIN
(Azithromycin 200 mg/5 mL powder for oral suspension)

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1. Name of the medicinal product

AZIN (Azithromycin) 200 mg/5 mL, powder for oral suspension.

2. Qualitative and quantitative composition

Each 5 mL of reconstituted suspension contains 200 mg of azithromycin (as azithromycin dihydrate).

Excipients with known effect:

Each 5 mL contains sucrose, aspartame (a source of phenylalanine), methyl parahydroxybenzoate and propyl parahydroxybenzoate (parabens).

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Powder for oral suspension.

A white, free-flowing powder with a characteristic pleasant odour, yielding a suspension after reconstitution.

4. Clinical particulars

4.1 Therapeutic indications

Azithromycin is indicated for the treatment of the following infections caused by susceptible organisms: upper respiratory tract infections, including pharyngitis, tonsillitis, sinusitis and otitis media; lower respiratory tract infections, including bronchitis and pneumonia; skin and soft-tissue infections; and uncomplicated genital infections due to Chlamydia trachomatis. Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology

Children over 6 months to 3 years (up to 15 kg): 10 mg/kg as a single daily dose for 3 days, measured with the dosing dropper provided (each 0.25 mL contains 10 mg of azithromycin). Children over 3 years or weighing more than 15 kg, using the measuring spoon provided: 15–25 kg — 5 mL once daily for 3 days; 26–35 kg — 7.5 mL once daily for 3 days; 36–45 kg — 10 mL once daily for 3 days; over 45 kg — the adult dose. In uncomplicated genital Chlamydia trachomatis infection, the adult dose is a single 1 g dose.

Method of administration

For oral use. Absorption of azithromycin is reduced by food; the suspension should therefore be taken at least 1 hour before or 2 hours after a meal. Shake well before use. See section 6.6 for reconstitution.

4.3 Contraindications

Hypersensitivity to azithromycin, erythromycin, any other macrolide or ketolide antibiotic, or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Hypersensitivity and serious skin reactions

As with erythromycin and other macrolides, serious allergic reactions including angioedema and anaphylaxis (rarely fatal), and severe cutaneous adverse reactions (SJS, TEN, DRESS, AGEP), have been reported. Some reactions with azithromycin have resulted in recurrent symptoms requiring a prolonged period of observation and treatment. If an allergic reaction occurs, the medicine should be discontinued and appropriate therapy instituted.

Hepatotoxicity

As the liver is the principal route of elimination, azithromycin should be used with caution in patients with significant hepatic disease; it is contraindicated in severe hepatic impairment. Cases of fulminant hepatitis potentially leading to life-threatening hepatic failure have been reported. Azithromycin should be stopped immediately if signs and symptoms of hepatitis occur.

QT prolongation

Prolonged cardiac repolarisation and QT interval, conferring a risk of cardiac arrhythmia and torsades de pointes, have been seen with macrolides including azithromycin. Caution is required in patients with congenital or documented QT prolongation, those taking other medicinal products known to prolong the QT interval, and those with electrolyte disturbance (particularly hypokalaemia or hypomagnesaemia), clinically relevant bradycardia, cardiac arrhythmia or severe cardiac insufficiency.

Other precautions

Clostridioides difficile-associated diarrhoea, ranging from mild to fatal colitis, should be considered in patients presenting with diarrhoea. Exacerbations of myasthenia gravis and new onset of myasthenic syndrome have been reported. Caution is advised in patients with severe renal impairment (GFR < 10 mL/min).

Excipients

This medicine contains sucrose; patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine, and sucrose may be harmful to the teeth. It contains aspartame, a source of phenylalanine, which may be harmful for people with phenylketonuria. It contains methyl and propyl parahydroxybenzoate, which may cause allergic reactions (possibly delayed).

4.5 Interaction with other medicinal products and other forms of interaction

Antacids: reduce peak serum concentrations of azithromycin by about 24%; azithromycin should be taken at least 1 hour before or 2 hours after an antacid. Digoxin: raised digoxin levels should be borne in mind. Ergot derivatives: concurrent use is not recommended owing to the theoretical possibility of ergotism. Coumarin anticoagulants: post-marketing reports of potentiated anticoagulation; monitoring of prothrombin time is advised. Ciclosporin: ciclosporin levels should be monitored and the dose adjusted. Azithromycin does not interact significantly with the hepatic cytochrome P450 system and does not undergo the interactions seen with erythromycin and other macrolides.

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal reproduction studies have shown no evidence of harm to the foetus, but there are no adequate and well-controlled studies in pregnant women; azithromycin should be used during pregnancy only if clearly needed.

Breast-feeding

Azithromycin is excreted in human breast milk; it should not be used in a nursing mother unless the potential benefits justify the potential risks to the infant.

4.7 Effects on ability to drive and use machines

There is no evidence to suggest that azithromycin may affect the ability to drive or operate machinery.

4.8 Undesirable effects

The adverse reactions are listed below by System Organ Class and frequency, defined as: common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000) and not known (cannot be estimated from the available data).

System Organ Class	Frequency	Adverse reaction
Infections and infestations	Uncommon	Candidiasis, oral candidiasis, vaginal infection, gastroenteritis
	Not known	Pseudomembranous colitis
Blood and lymphatic system disorders	Uncommon	Leukopenia, neutropenia, eosinophilia
	Not known	Thrombocytopenia, haemolytic anaemia
Immune system disorders	Uncommon	Angioedema, hypersensitivity
	Not known	Anaphylactic reaction
Psychiatric disorders	Uncommon	Nervousness, insomnia
	Not known	Agitation, aggression, anxiety, delirium, hallucination
Nervous system disorders	Common	Headache
	Uncommon	Dizziness, somnolence, dysgeusia, paraesthesia
	Not known	Syncope, convulsions, hypoaesthesia, psychomotor hyperactivity, anosmia, ageusia, myasthenia gravis aggravated
Ear and labyrinth disorders	Uncommon	Vertigo
	Not known	Hearing impairment including deafness and/or tinnitus
Cardiac disorders	Uncommon	Palpitations
	Not known	Torsades de pointes, arrhythmia including ventricular tachycardia, electrocardiogram QT prolonged
Vascular disorders	Not known	Hypotension
Gastrointestinal disorders	Common	Diarrhoea, abdominal pain, nausea, flatulence
	Uncommon	Vomiting, dyspepsia, constipation, gastritis
	Not known	Pancreatitis, tongue discolouration
Hepatobiliary disorders	Uncommon	Hepatitis
	Rare	Hepatic function abnormal
	Not known	Hepatic failure, fulminant hepatitis, cholestatic jaundice
Skin and subcutaneous tissue disorders	Uncommon	Rash, pruritus, urticaria, dermatitis, dry skin
	Rare	Photosensitivity reaction
	Not known	Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalised exanthematous pustulosis (AGEP), erythema multiforme
Musculoskeletal and connective tissue disorders	Uncommon	Osteoarthritis, myalgia, back pain, neck pain
	Not known	Arthralgia
Renal and urinary disorders	Uncommon	Dysuria, renal pain
	Not known	Interstitial nephritis, acute renal failure
General disorders and administration site	Common	Fatigue

System Organ Class	Frequency	Adverse reaction
conditions		
	Uncommon	Chest pain, oedema, malaise, asthenia
Investigations	Uncommon	Aspartate aminotransferase increased, alanine aminotransferase increased, blood bilirubin increased, blood urea increased, blood creatinine increased

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the National Regulatory Authority.

4.9 Overdose

Adverse events at higher-than-recommended doses were similar to those seen at normal doses. Typical symptoms of overdose with macrolide antibiotics include reversible loss of hearing, severe nausea, vomiting and diarrhoea. In the event of overdose, activated charcoal and general symptomatic and supportive measures are indicated as required.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use, macrolides. ATC code: J01FA10.

Azithromycin is a macrolide antibiotic of the azalide subclass. Its mechanism of action is based on the suppression of bacterial protein synthesis by binding to the 50S ribosomal subunit and inhibiting peptide translocation. Resistance may be inherent or acquired, the main mechanisms being target-site alteration, altered antibiotic transport and modification of the antibiotic; complete cross-resistance exists among Streptococcus pneumoniae, group A beta-haemolytic streptococci, Enterococcus faecalis and Staphylococcus aureus (including MRSA) to erythromycin, azithromycin, other macrolides and lincosamides. The prevalence of acquired resistance may vary geographically and with time, and local information on resistance is desirable.

5.2 Pharmacokinetic properties

The oral bioavailability of azithromycin is approximately 37%, with peak plasma levels reached 2–3 hours after administration. Azithromycin is extensively distributed throughout the body, with tissue concentrations up to 50 times the plasma concentration, indicating extensive tissue binding; the steady-state volume of distribution is about 31 L/kg. Serum protein binding is variable and concentration-dependent (12–52%). The terminal plasma elimination half-life is 2 to 4 days. Azithromycin is excreted largely unchanged, predominantly in the bile, with about 12% of a dose excreted unchanged in the urine; its metabolites are microbiologically inactive.

5.3 Preclinical safety data

In animal studies at high multiples of the clinical dose, azithromycin caused reversible phospholipidosis; the relevance to humans is unknown. Electrophysiological studies have shown that azithromycin prolongs the QT interval. There was no evidence of genotoxic potential, and no teratogenic effects were observed in embryotoxicity studies in mice and rats.

6. Pharmaceutical particulars

6.1 List of excipients

- Sucrose
- Methyl parahydroxybenzoate
- Propyl parahydroxybenzoate

- Sodium saccharin
- Xanthan gum
- Sodium chloride
- Tribasic sodium phosphate (anhydrous)
- Aspartame
- Colloidal silicon dioxide
- Menthol flavour
- Banana flavour
- Vanilla flavour

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months (unopened). After reconstitution, the suspension should be used within 5 days.

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture. After reconstitution, store below 30°C and discard any unused suspension after 5 days. Keep out of the reach and sight of children.

6.5 Nature and contents of container

Amber glass bottle with an aluminium/PP cap, delivering 15 mL of suspension after reconstitution, presented in a carton with a dosing dropper/measuring spoon and the package insert.

6.6 Special precautions for disposal and other handling

Reconstitution: add the volume of previously boiled and cooled water indicated on the label, then shake well until a uniform suspension is obtained. Shake well before each use. Discard any suspension remaining 5 days after reconstitution.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorisation Holder and Manufacturer

The ACME Laboratories Ltd., Dhaka-1207, Bangladesh.

8. Marketing Authorisation Number

H2009/20067/143

9. Date of first authorisation / renewal of the authorisation

10. Date of revision of the text