SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product:

AZITCOR-500 (Azithromycin tablets USP 500 mg)

2. Qualitative and Quantitative Composition:

Each Film-coated tablet contains Azithromycin (as Azithromycin Dihydrate) 500mg
For a full list of excipients, see section 6.1

3. Pharmaceutical Form: Tablet

White, oblong, film coated tablets having a break line on one side and plain on other side.

4. Clinical Particulars:

4.1 Therapeutic indications:

Azithromycin is indicated for the following bacterial infections induced by micro-organisms susceptible to azithromycin:

- Acute bacterial sinusitis (adequately diagnosed)
- Acute bacterial otitis media (adequately diagnosed)
- Pharyngitis, tonsillitis
- Acute exacerbation of chronic bronchitis (adequately diagnosed)
- Mild to moderately severe community acquired pneumonia
- Infections of the skin and soft tissues of mild to moderate severity e.g. folliculitis, cellulitis, erysipelas
- Uncomplicated Chlamydia trachomatis urethritis and cervicitis

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Children and adolescents with a body weight above 45 kg, adults and the elderly: The total dose is 1500 mg, administered as 500 mg once daily for 3 days. Alternatively, the same total dose (1500 mg) can be administered in a period of 5 days, 500 mg on the first day and 250 mg on day 2 to 5.

In the case of uncomplicated *Chlamydia trachomatis* urethritis and cervicitis, the dosage is 1000 mg as a single oral dose.

Children and adolescents with a body weight below 45 kg: Azithromycin tablets are not suitable for patients under 45 kg body weight. Other dosage forms are available for this group of patients.
Elderly patients: For elderly patients the same dose as for adults can be applied.
Patients with renal impairment: Dose adjustment is not required in patients with mild to moderate renal impairment (GFR 10-80 ml/min).
Patients with hepatic impairment: Dose adjustment is not required for patients with mild to moderate hepatic dysfunction.

Method of administration
For oral administration only.
The tablets can be taken with or without food.
The tablets should be taken with ½ glass of water.

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

4.4 Special warnings and precautions for use
As with erythromycin and other macrolides, rare serious allergic reactions including angioneurotic oedema and anaphylaxis (rarely fatal), have been reported. Some of these reactions have resulted in recurrent symptoms and required a longer period of observation and treatment.
Since the liver is the principal route of elimination for azithromycin, the use of azithromycin should be undertaken with caution in patients with significant hepatic disease. Cases of fulminant hepatitis potentially leading to life-threatening liver failure have been reported with azithromycin. Some patients may have had pre-existing hepatic disease or may have been taking other hepatotoxic medicinal products.
In case of signs and symptoms of liver dysfunction, such as rapid developing asthenia associated with jaundice, dark urine, bleeding tendency or hepatic encephalopathy, liver function tests/investigations should be performed immediately. Azithromycin administration should be stopped if serious liver dysfunction emerges.

As with any antibiotic preparation, it is recommended to pay attention to signs of superinfection with non-susceptible micro-organisms like fungi. A superinfection may require an interruption of the azithromycin treatment and initiation of adequate measures.

Clostridium difficile associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including azithromycin, and may range in severity from mild diarrhoea to fatal colitis. 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 antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who are present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

Prolonged cardiac repolarisation 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 repolarisation. Therefore, caution is required when treating patients:

• With congenital or documented acquired QT prolongation.

• Currently receiving treatment with other active substances known to prolong QT interval such as antiarrhythmics of classes IA and III, cisapride and terfenadine.

• With electrolyte disturbance, particularly in cases of hypokalaemia and hypomagnesaemia

• With clinically relevant bradycardia, cardiac arrhythmia or severe cardiac insufficiency

4.5 Interaction with other medicinal products and other forms of interaction

Antacids: In a pharmacokinetic study to the effect of co-administration of antacids and azithromycin, no effect on the total bioavailability was seen, although the peak serum levels were reduced by approximately 25%. Azithromycin must be taken at least 1 hour before or 2 hours after antacids.

Digoxin: Some of the macrolide antibiotics have been reported to impair the microbial metabolism of digoxin in the gut in some patients. In patients receiving concomitant azithromycin, a related azalide antibiotic, and digoxin the possibility of increased digoxin levels should be borne in mind.

Zidovudine: Single 1000 mg doses and multiple doses of 600 mg or 1200 mg azithromycin had little effect on the plasma pharmacokinetics or renal excretion of zidovudine or its glucuronide metabolite. However, administration of azithromycin increased the concentrations of phosphorylated zidovudine, the clinically active metabolite, in peripheral blood mononuclear cells. The clinical significance of this finding is unclear, but it may be of benefit to patients.

Azithromycin does not interact significantly with the hepatic cytochrome P450 system. It is not believed to undergo pharmacokinetic drug interactions as seen with erythromycin and other

macrolides. Hepatic cytochrome P450 induction or inactivation via cytochrome-metabolite complex does not occur with azithromycin.

Ergotamine derivatives: Due to the theoretical possibility of ergotism, the concurrent use of azithromycin with ergot derivatives is not recommended.

Pharmacokinetic studies have been conducted between azithromycin and the following drugs known to undergo significant cytochrome P450 mediated metabolism.

Astemizole, alfentanil: There are no known data on interactions with astemizole or alfentanil. Caution is advised in the co-administration of these medicines with Azithromycin because of the known enhancing effect of these medicines when used concurrently with the macrolid antibiotic erythromycin.

Cisapride: Cisapride is metabolized in the liver by the enzyme CYP 3A4. Because macrolides inhibit this enzyme, concomitant administration of cisapride may cause the increase of QT interval prolongation, ventricular arrhythmias and torsades de pointes.

Coumarin-Type Oral Anticoagulants: In a pharmacokinetic interaction study, azithromycin did not alter the anticoagulant effect of a single 15-mg dose of warfarin administered to healthy volunteers. There have been reports received in the post-marketing period of potentiated anticoagulation subsequent to co-administration of azithromycin and coumarin-type oral anticoagulants. Although a causal relationship has not been established, consideration should be given to the frequency of monitoring prothrombin time when azithromycin is used in patients receiving coumarin-type oral anticoagulants.

Cyclosporin: In a pharmacokinetic study with healthy volunteers that were administered a 500 mg/day oral dose of azithromycin for 3 days and were then administered a single 10 mg/kg oral dose of cyclosporin, the resulting cyclosporin Cmax and AUC0-5 were found to be significantly elevated.

Consequently, caution should be exercised before considering concurrent administration of these drugs. If co-administration of these drugs is necessary, cyclosporin levels should be monitored and the dose adjusted accordingly.

Fluconazole: Co-administration of a single dose of 1200 mg azithromycin did not alter the pharmacokinetics of a single dose of 800 mg fluconazole. Total exposure and half-life of azithromycin were unchanged by the co-administration of fluconazole, however, a clinically insignificant decrease in Cmax (18%) of azithromycin was observed.

Theophylline: There is no evidence of a clinically significant pharmacokinetic interaction when azithromycin and theophylline are co-administered to healthy volunteers. As interactions of other

macrolides with theophylline have been reported, alertness to signs that indicate a rise in theophylline levels is advised.

4.6 Fertility, Pregnancy and Lactation

Pregnancy: There are no adequate data from the use of azithromycin in pregnant women. In reproduction toxicity studies in animals azithromycin was shown to pass the placenta, but no teratogenic effects were observed. The safety of azithromycin has not been confirmed with regard to the use of active substances during pregnancy. Therefore, Azithromycin should only be used during pregnancy if definitely indicated.

Lactation: Azithromycin passes into breast milk. Because it is not known whether azithromycin may have adverse effects on the breast-fed infant, nursing should be discontinued during treatment with Azithromycin. Among other things diarrhoea, fungus infection of the mucous membrane as well as sensitization is possible in the nursed infant. It is recommended to discard the milk during treatment and up until 2 days after discontinuation of treatment. Nursing may resume thereafter.

Fertility: Animal data do not suggest an effect of the treatment of azithromycin on male and female fertility. Human data are lacking.

4.7 Effects on ability to drive & use machines

No data are available regarding the influence of azithromycin on a patient's ability to drive or operate machinery. However, the possibility of undesirable effects like dizziness and convulsions should be taken into account when performing these activities.

4.8 Undesirable Effects

The table below lists the adverse reactions identified through clinical trial experience and postmarketing surveillance by system organ class and frequency. Adverse reactions identified from postmarketing experience are included in italics. The frequency grouping is defined using the following convention: Very common (≥1/10); Common (≥ 1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥ 1/10,000 to <1/1,000); Very Rare (< 1/10,000); and Not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

very common	common	uncommon	rare	very rare	not known
Infections and infestations					
		Candidiasis Oral candidiasis Vaginal infection			Pseudomembranous colitis
Blood and lymphatic system disorders					
	Lymphocyte count decreased, eosinophil count increased	Leukopenia Neutropenia			Thrombocytopenia, Haemolytic anaemia
Immune system disorders					
		Angioedema Hypersensitivity			Anaphylactic reaction
Metabolism and nutrition disorders					
	anorexia				
Nervous system disorders					
	Dizziness Headache Paraesthesia Dysgeusia	Hypoaesthesia Somnolence Insomnia			Syncope,Convulsion, Psychomotor hyperactivity, Anosmia, Ageusia, Parosmia, Myasthenia gravis
Eye disorders					
	Visual impairment				
Ear and labyrinth disorders					
	Deafness	Hearing impaired, tinnitus	Vertigo		

Cardiac disorders					
		Palpitations			Torsades de pointes Arrhythmia including ventricular tachycardia. Electrodiogram QT prolonged
Vascular disorders					
					Hypotension
Gastrointestinal disorders					
Diarrhoea, Abdominal pain, Nausea, Flatulence	Vomiting Dyspepsia	Gastritis Constipation			Pancreatitis, Tongue and teeth discoloration
Hepatobiliary disorders					
		Hepatitis, aspartate aminotransferase increased, alanine aminotransferase increased, blood bilirubine increased	Hepatic function abnormal		Hepatic failure*, Hepatitis fulminant, Hepatic necrosis, Jaundice cholestatic
Skin and subcutaneous tissue disorders					
	Rash, Pruritis	Stevens-Johnson syndrome, Photosensitivity reaction, Urticaria	allergic reactions including angioneurotic oedema,		Toxic epidermal necrolysis, Erythema multiforme
Musculoskeletal and connective tissue disorders					

	Arthralgia				
Renal and urinary disorders					
		Blood urea increased	Renal failure acute, Nephritis interstitial		
General disorders and administration site conditions					
	Fatigue	Chest pain Oedema Malaise Asthenia			
Investigations					
	Lymphocyte count decreased, eosinophil count increased, blood bicarbonate decreased	blood creatinine increased, blood potassium abnormal			

*which has rarely resulted in death

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions to the National Regulatory Agents.

4.9 Overdose:

Adverse events experienced in higher than recommended doses were similar to those seen at normal doses.

Symptoms: The typical symptoms of an overdose with macrolid antibiotics include reversible loss of hearing, severe nausea, vomiting and diarrhoea.

Treatment: In the event of overdose, general symptomatic and supportive measures are indicated as required.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Azithromycin is a macrolid antibiotic belonging to the azalide group.

The molecule is constructed by adding a nitrogen atom to the lactone ring of erythromycin A. The chemical name of azithromycin is 9-deoxy-9a-aza-9a-methyl-9a-homoerythromycin A. The molecular weight is 749.0.

Mode of action: Azithromycin is an azalide, a sub-class of the macrolid antibiotics. By binding to the 50S ribosomal sub-unit, azithromycin avoids the translocation of peptide chains from one side of the ribosome to the other. As a consequence of this, RNA-dependent protein synthesis in sensitive organisms is prevented.

PK/PD relationship: For azithromycin the AUC/MIC is the major PK/PD parameter correlating best with the efficacy of azithromycin.

Mechanism of resistance: Resistance to azithromycin may be inherent or acquired. There are three main mechanisms of resistance in bacteria: target site alteration, alteration in antibiotic transport and modification of the antibiotic.

Complete cross resistance exists among *Streptococcus pneumoniae*, beta haemolytic streptococcus of group A, *Enterococcus faecalis* and *Staphylococcus aureus*, including methicillin resistant *S. aureus* (MRSA) to erythromycin, azithromycin, other macrolides and lincosamides.

Breakpoints: EUCAST (European Committee on Antimicrobial Susceptibility Testing)

	MIC breakpoint (mg/L)	
Pathogens	**Susceptible (mg/L)**	**Resistant (mg/L)**
Staphylococcus spp.	≤ 1	> 2
Streptococcus spp. (Group A, B, C, G)	≤ 0.25	> 0.5
Streptococcus pneumoniae	≤ 0.25	> 0.5
Haemophilus influenzae	≤ 0.125	> 4
Moraxella catarrhalis	≤ 0.25	> 0.5
Neisseria gonorrhoeae	≤ 0.25	> 0.5

Susceptibility: The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.
Pathogens for which resistance may be a problem: prevalence of resistance is equal to or greater than 10% in at least one country in the European Union.

Table of susceptibility

Commonly susceptible species
Aerobic Gram-negative microorganisms
*Haemophilus influenzae**
*Moraxella catarrhalis**
Other microorganisms
Chlamydophila pneumoniae
Chlamydia trachomatis
Legionella pneumophila
Mycobacterium avium
*Mycoplasma pneumonia**
Species for which acquired resistance may be a problem
Aerobic Gram-positive microorganisms
*Staphylococcus aureus**
Streptococcus agalactiae
*Streptococcus pneumoniae**

*Streptococcus pyogenes**
Other microorganisms
Ureaplasma urealyticum
Inherently resistant organisms
Aerobic Gram-positive microorganisms
Staphylococcus aureus – methicillin resistant and erythromycin resistant strains
Streptococcus pneumoniae – penicillin resistant strains
Aerobic Gram-negative microorganisms
Escherichia coli
Pseudomonas aeruginosa
Klebsiella spp.
Anaerobic Gram-negative microorganisms
Bacteroides fragilis-group

* Clinical effectiveness is demonstrated by sensitive isolated organisms for approved clinical indications.

5.2 Pharmacokinetic Properties

Absorption: Bioavailability of azithromycin after oral administration is approximately 37%. Peak plasma concentrations are attained after 2-3 hours. The mean maximum concentration observed (Cmax) after a single dose of 500 mg is approximately 0.4 µg/ml.

Distribution: Orally administered azithromycin is widely distributed throughout the body. Pharmacokinetic studies have demonstrated that the concentrations of azithromycin measured in tissues are noticeably higher (up to 50 times the maximum observed concentration in plasma) than those measured in plasma. This indicates that the agent strongly binds to tissues (steady-state distribution volume approx. 31 l/kg).

At the recommended dose no accumulation appears in the serum. Accumulation appears in tissues were levels are much higher than in serum. Three days after administration of 500 mg as a single dose or in partial doses concentrations of 1,3-4,8 µg/g, 0,6-2,3 µg/g, 2,0-2,8 µg/g and 0-0,3 µg/ml have been measured in resp. lung, prostate, tonsil and serum.

In experimental *in vitro* and *in vivo* studies azithromycin accumulates in phagocytes. Release is stimulated by active phagocytosis. In animal models this process contributes to the accumulation of azithromycin in tissue.

Binding of azithromycin to serum proteins is variable and varies from 52% at 0,05 mg/l to 18% at 0,5 mg/l, depending on the serum concentration.

Excretion: The terminal plasma elimination half-life closely reflects the elimination half-life from tissues of 2-4 days.
Approximately 12% of an intravenously administered dose is excreted in unchanged form with the urine over a period of 3 days; the major proportion in the first 24 hours. Concentrations of up to 237 µg/ml azithromycin, 2 days after a 5-day course of treatment, have been found in human bile. Ten metabolites have been identified (formed by N- and O-demethylation, by hydroxylation of the desosamine and aglycone rings, and by splitting of the cladinose conjugate). Investigations suggest that the metabolites do not play a role in the microbiological activity of azithromycin.

Pharmacokinetics in Special populations:

Renal Insufficiency: Following a single oral dose of azithromycin 1 g, mean Cmax and AUC0-120 increased by 5.1% and 4.2% respectively, in subjects with mild to moderate renal impairment (glomerular filtration rate of 10-80 ml/min) compared with normal renal function (GFR > 80ml/min). In subjects with severe renal impairment, the mean Cmax and AUC0-120 increased 61% and 35% respectively compared to normal.

Hepatic insufficiency: In patients with mild to moderate hepatic impairment, there is no evidence of a marked change in serum pharmacokinetics of azithromycin compared to normal hepatic function. In these patients, urinary recovery of azithromycin appears to increase perhaps to compensate for reduced hepatic clearance.

Elderly: The pharmacokinetics of azithromycin in elderly men was similar to that of young adults; however, in elderly women, although higher peak concentrations (increased by 30-50%) were observed, no significant accumulation occurred.

Infants, toddlers, children and adolescents: Pharmacokinetics has been studied in children aged 4 months – 15 years taking capsules, granules or suspension. At 10 mg/kg on day 1 followed by 5

mg/kg on days 2-5, the Cmax achieved is slightly lower than in adults, with 224 µg/l in children aged 0.6-5 years and after 3 days dosing, and 383 µg/l in those aged 6-15 years. The half-life of 36 h in the older children was within the expected range for adults.

5.3 Preclinical safety Data:

In animal studies using exposures 40 times those achieved at the clinical therapeutic dosages, azithromycin was found to have caused reversible phospholipidosis, but as a rule there were no associated toxicological consequences. The relevance of this finding to humans receiving azithromycin in accordance with the recommendations is unknown.

Electrophysiological investigations have shown that azithromycin prolongs the QT interval.

Carcinogenic potential: Long-term studies in animals have not been performed to evaluate carcinogenic potential.

Mutagenic potential: There was no evidence of a potential for genetic and chromosome mutations in in-vivo and in-vitro test models.

Reproductive toxicity: Teratogenic effects were not observed in rat reproductive toxicity studies. In rats, azithromycin dosages of 100 and 200 mg/kg bodyweight/ day led to mild retardation in foetal ossification and in maternal weight gain. In peri- and postnatal studies in rats mild retardations in physical and reflex development were noted following treatment with 50 mg/kg/day azithromycin and above.

6. Pharmaceutical Particulars:

6.1 List of excipients:

Sr. No.	Name of Excipients	Specification
1.	Macrogol-6000	BP
2.	Hydroxypropyl Cellulose (Klucel LF)	BP
3.	Isopropyl alcohol	BP
4.	Dichloromethane	BP
5.	Maize Starch	BP
6.	Microcrystalline Cellulose	BP
7.	Sodium Methyl Paraben	BP
8.	Sodium Propyl Paraben	BP
9.	Purified Water	BP
10.	Croscarmellose Sodium	BP
11.	Magnesium Stearate	BP
12.	Sodium Lauryl Sulfate	BP
13.	Purified talc	BP
14.	Idealcoat IJ–MS-1011 (White)	IH
15.	Purified talc	BP
16.	Macrogol - 400	BP

6.2 Incompatibilities: Not applicable

6.3 Shelf life: 36 Months

6.4 Special precautions for storage:

Store below 30°C in dry place. Protect from light.

Keep medicine out of reach of children.

6.5 Nature and contents of container:

3 tablets are packed in Alu-Alu blister.

Such 1 blister to be packed in a carton along with a pack insert.

6.6 Special Precaution for Disposal and other handling: Not applicable

7. Marketing Authorization Holder and Manufacturing Site Addresses:

Company name: Signature Healthcare Ltd.

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8. Marketing Authorization Numbers:
CTD13449

9. Date of first Registration /renewal of the Registration:

12/06/2026

10. Date of revision of the text: Not Applicable

12/06/2026