Summary Product Characteristics (SmPC)	
1	**NAME OF THE FINISHED PHARMACEUTICAL PRODUCT**
1.1	**Product Name :** Zaha
1.2	**Strength :** Azithromycin Oral Suspension 200 mg / 5 mL
1.3	**Pharmaceutical Dosage Form :** Suspension
2.	**QUALITATIVE AND QUANTITATIVE COMPOSITION**
2.1	**Qualitative Declaration** Each 5 mL contains: Azithromycin Dihydrate USP equivalent to Azithromycin.....200 mg
2.2	**Qualitative & Quantitative Composition:**

Sr. No.	Ingredients	Quantity per 5 mL in mg
1	Azithromycin Dihydrate USP	207.41
2	Sucrose BP (Pharma Grade Sugar)	2000.00
3	Sodium Methyl Hydroxybenzoate BP	9.00
4	Sodium Propyl Hydroxybenzoate BP	1.00
5	Xanthan Gum USP NF	25.00
6	Propylene Glycol BP	250.00
7	Citric Acid Monohydrate BP	3.75
8	Liquid Sorbitol (Non-crystallising) BP	1500.00
9	Levomenthol BP	0.15
10	Saccharin Sodium BP	15.00
11	Quinioline Yellow WS IH	1.00
12	Peppermint Oil RSPP IH	0.01 mL
13	Purified Water @	q.s. to 5 mL

*Qty to be added on 100% assay as follows;

Actual quantity required = Theoretical quantity x $\frac{100}{\text{Assay on anhydrous basis}}$

@ Purified Water complies with the specifications of USP-NF/BP /Ph. Eur./Ph.Int./IH/IP

	BP : British Pharmacopoeia USPNF : United States Pharmacopeia National Formulary USP : United States Pharmacopeia Ph. Eur. : European Pharmacopoeia Ph.Int. : International Pharmacopoeia IH : In-house Specification IP : Indian Pharmacopoeia
3	**PHARMACEUTICAL FORM** Light yellow coloured suspension, with characteristic taste and odour
4	**CLINICAL PARTICULARS** **4.1 Therapeutic Indications:** Zaha is indicated for the treatment of patients with mild to modrate infections caused by susceptible strains of the designated microoragnism in the specific conditions listed below **Children:** Acute otitis media caused by Haemophilus influenzae, Moraxella Catarrhalis or Streptococcus pneumoniae. Community-acquired pneumonia due to Chlamydia pneumoniae, Haemophilus influenzae, Mycoplasma pneumoniae or Streptococcus pneumoniae in patients appropriate for oral therapy. Pharyngitis/tonsillitis caused by Streptococcus pyogenes as an alternative to first-line therapy in individuals who cannot use first – line therapy.
	4.2 Posology and method of administration For oral use. **Children:** Azithromycin for oral suspension can be taken with or without food. **Acute Otitis Media :** The recommended dose of azithromycin for oral suspension for the treatment of children with acute otitis media is 30 mg/kg given as a single dose on the first day followed by 5 mg/kg/day on Days two through five. **Community-Acquired Pneumonia:** The recommended dose of azithromycin oral suspension is 10 mg/kg as a single dose on the first day followed by 5 mg/kg on Days 2 through 5. The safety of re-dosing azithromycin in children who vomit after receiving 30 mg/kg as a single dose has not been established. In clinical studies involving 487 patients with acute otitis media given a single 30 mg/kg dose of azithromycin, eight patients who vomited within 30 minutes of dosing were re-dosed at the same total dose. **Pharyngitis/Tonsillitis :** The recommended dose of azithromycin for children with pharyngitis/tonsillitis is 12 mg/kg once daily for 5 days.
	4.3 Contraindications: Azithromycin is contraindicated in patients with known hypersensitivity to azithromycin, erythromycin or any macrolide antibiotic.

4.4 Special warning and precautions for use:

Warnings

Serious allergic reactions, including angiodema, anaphylaxis, and dermatologic reactions including Stevens Johnsons Syndrome and toxic epidermal necrolysis have been reported rarely in patients on azithromycin therapy. Although rare, fatalities have been reported. Despite initially successful symptomatic treatment of the allergic symptomatic therapy was discontinued, the allergic symptoms recurred soon thereafter in some patients without these patients required prolonged periods of obsevation and symptomatic treatment. The relationship of these episodes to the long tissue half-life of azithromycin and subsequent prolonged exposure to antigen is unknown at present. If an allergic reaction occurs, the drug should be discontinued and appropriate therapy should be instituted.

Physicians should be aware that reappearance of the allergic symptoms may occur when symptomatic therapy is discontinued. W Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by Clostridum difficile is a primary cause of "antibiotic-associated colitis." After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to discontinuation of the drug alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against Clostridium diffcile colitis.

Precautions

General : Because azithromycin is principally eliminated via the liver, caution should be exercised when azithromycin is administered to patients with 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. The following adverse events have been reported in clinical trials with azithromycin, an azalide; however, they have been reported with macrolide products: ventrricular arrhythmias,incullding ventricular tachycardia and torsade de pointes, in individuals with prolonged QT intervals. There has been a spontaneous report from the post marketing exprience of a patients with previous history of arrhythmias who experienced torsade de pointes and subsequent myocardial infarction following a course of azithromycin therapy.

4.5 Interactions with other medicinal products and other forms of Interactions :

Co-administration of nelfinavir at steady state with a single oral dose of azithromycin serum concentrations. Azithromycin did not affect the prothrombin time response to a single dose of warfarin. However, prudent medical practise dictates careful monitoring of prothrombin time in all patients treated with azithromycin and warfarin concomitantly. Concurrent use of macrolides and warfarin in clinical pratice has been associated with increased anticoagulant effects.

4.6 Pregnancy and Lactation:

Pregnancy : Teratogenic Effects. Pregnancy Category B:

Azithromycin should be used during Pregnancy only if clearly needed .

	Paediatric Use : Acute Otitis Media (dosage regimen : 10 mg/kg on Day 1 followed by 5mg/kg on days 2-5) : Safety and effectiveness in the treatment of children with otitis media under 6 month of age have not been established. Community-Aquired Pneumonia (dosage regimen : 10 mg/kg on Day 1 followed by 5 mg/kg on Days 2-5) : Safety and effectiveness in the treatment of children with community-acquired pneumonia under 6 months of age have not been established. Safety and effectiveness for pneumoniae were documented in pediatric clinical trials. Safety and effectiveness for pneumonia due to Haemophilus influenzae and Streptococcus pneumoniae were not documented bacteriologically in the pediatric clinical trial due to difficulty in obtaining specimens. Use of azithromycin for these two microorganisms is supported, however, by evidence from adequate and well-controlled studies in adults. Pharyngitis/Tonsillitis (dosage regimen:12 mg/kg on Days 1-5): Safety and effectiveness in the treatment of children with pharyngitis/tonsillitis under 2 years of age have not been established
	4.7 Effects on ability to drive and use machine: There is no evidence to suggest that azithromycin may have an effect on a patient's ability to drive or operate machinery.
	4.8 Undesirable Effects: In Clinical trials, most of the reported side effects were mild to moderate in severity and were reversible upon discontinuationof the drug. Potentially serious side effects of angioedema and cholestatic jaundice were reported rarely. Most of the side effects leading to discontinuation were related to the gastrointestinal tract, e.g., nausea, vomiting, diarrhea, or abdominal pain Laboratory Abnormalities : Clinically signifacant abnormalities (irrespective of drug relationship) occuring during the clinical trials were reported as follows: with an incidence of greater than 1% decreased hemoglobin, hematocrit, lymphocytes and blood glucose; elevated serum creatine phosphoinase, potassium, ALT(SGPT), GGT, and AST(SGOT), BUN, creatinine, blood glucose, platelet count, eosinophils; with an incidence of less than 1% leukopenia, neutropenia, decreased platelet count; elevated serum alkaline phosphatase, bilirubin, LDH and phosphate. The majority of subjects with elevated serum creatinine also had abnormal values at baseline.
	4.9 Overdosage: Adverse events experienced in higher than recommended doses were similar to those seen at normal doses. In the event of overdosage, general symptomatic and supportive measures are indicated as required.

5.	**PHARMACOLOGICAL PROPERTIES** **Pharmacological Classification** Antibiotic **5.1 Pharmacodynamic Properties** Azithromycin acts by binding to the 50S ribosomal subunit of susceptible microorganisms and, thus, interfering with microbial protein synthesis. Nucleic acid synthesis is not affected. Azithromycin concentrates in phagocytes and fibroblasts. In vivo studies suggest that concentration in phagocytes may contribute to drug distribution to inflamed tissues. Azithromycin has been shown to be active against most isolates of the following microorganisms,both in vitro and in clinical infections as described in the INDICATIONS AND USAGE section. **Aerobic and facultative gram-positive microorganisms** *Staphylococcus aureus* *Streptococcus agalactiae* *Streptococcus pneumoniae* *Streptococcus pyogenes* NOTE: Azithromycin demonstrates cross-resistance with erythromycin-resistant gram-positive strains. Most strains of Enterococcus faecalis and methicillin-resistant staphylococci are resistant to azithromycin. **Aerobic and facultative gram-negative microorganisms** *Haemophilus ducreyi* *Haemophilus influenzae* *Moraxella catarrhalis* *Neisseria gonorrhoeae* "Other" microorganisms Chlamydia pneumoniae Beta-lactamase production should have no effect on azithromycin activity.
	5.2 Pharmacokinetics Properties: ***Absorption*** Biioavailibility afetr oral administration is approximately 37%. Peak concentrations in the plasma are attained 2-3 hours afetr taking the medicinal product. The AUC of azithromycin was unaffected by co-administration of an antacid containing aluminum and magnesium hydroxide with azithromycin capsules;,however,the Cmax was reduced by 24% ***Distribution*** The serum protein binding of azithromycin is variable in the Concentration range approximating human exposure, decreasing from 51 % at 0.02 µg/mL to 7% at 2 µg/mL. Greater azithromycin concentrations in tissues than in plasma or serum were observed. Tthe antimicrobial activity of azithromycin is pH related and appears to be reduced with decreasing pH. However, the extensive distribution of drug to tissues may be relevant to clinical activity.

Metabolism
Metabolism is predominatly hepatic (to inactive ,etabolites), with billiary excretion a major pathway of elimination.

Excretion
Elimination terminal elimination half –life of 68 hours. The prolonged terminal half-life is thought to be due to extensive uptake and subsequent release of drug from tissues. Biliary excretion of azithromycin, predominantly as unchanged drug, is a major route of elimination. Over the course of a week, approximately 6% of the administered dose appears as unchanged drug in urine

Special Populatons
Renal Insufficiency
The mean Cmax and AUC 0-120 increased 61% and 35%, respectively in subjects with severe renal impairment.
Hepatic Insufficiency
The pharmacokinetics of azithromycin in subjects with hepatic Impairment has not been established.

Pediatric patients
In two clinical studies, azithromycin for oral suspension was dosed at 10 mg/Kg on day 1, followed by 5 mg/Kg on days 2 through 5 to two groups of children (aged 1-5 years and 5-15 years, respectively).The mean pharmacokinetic parameters on day 5 were Cmax=0.216 mg/mL, Tmax=1.9 hours, and AUC0- 24=1.822 mg.hr/mL for the 1-to 5-year-old group and were Cmax=0.383 mg/mL, Tmax=2.4 hours,and AUC0-24=3.109 mg.hr/mL for the 5-to 15- year-old group.

5.3 Preclinical safety Data
In animal tests in which the dosages used amounted to 40 times the clinical therapeutic dosages, azithromycin was found to have caused reversible phospholipidosis, but as a rule no true toxicological consequences were observed which were associated with this. 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.

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

Reproductive toxicity:
In embryotoxicity studies in mice and rats no teratogenic effects were observed. In rats, azithromycin dosages of 100 and 200 mg/kg bodyweight/day led to slight retardations in fetal ossification and in maternal weight gain. In peri-/postnatal studies in rats, slight retardations in physical development and delay in reflex development were observed following treatment with 50 mg/kg/day azithromycin and above.

6.	**PHARMACEUTICAL PARTICULARS** **6.1 List of excipients** Sucrose BP (Pharma Grade Sugar) Sodium Methyl Hydroxybenzoate BP Sodium Propyl Hydroxybenzoate BP Xanthan Gum USP NF Propylene Glycol BP Citric Acid Monohydrate BP Liquid Sorbitol (Non-crystallising) BP Levomenthol BP Saccharin Sodium BP Quinioline Yellow WS IH Peppermint Oil RSPP IH Purified Water @
	6.2 Incompatibilities None known
	6.3 Shelf life 24 months from the date of manufacture
	6.4 Special precautions for storage Store below 25°C.
	6.5 Nature and contents of container A carton containing a bottle of 15 mL along with pack insert.
	6.6 Special precautions for disposal Not Applicable.
7.	**NAME AND ADDRESS OF MANUFACTURER** Ajanta Pharma Limited Ajanta House, Charkop, Kandivli (West) Mumbai-400 067 Country: India Telephone: 91 - 022-66061000 Telefax: 91 - 022-66061200/300 E-Mail: info@ajantapharma.com
8.	**REGISTRATION NUMBER** First time Application
9.	**CATEGORY FOR DISTRIBUTION** Prescription Preparation (P.P.)
10.	**DATE OF PUBLICATION OF THIS SmPC** July 2014