SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

AZISURE (AZITHROMYCIN FOR ORAL SUSPENSION USP 200 MG/5 ML)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition
Each 5 ml after reconstitution contains:
Azithromycin Dihydrate USP
Eq. to Azithromycin base 200 mg
Excipients Q.S.

Sr. No.	Ingredients	Spec	Qty. per bottle (gm)/30 ml	Category
1.	* Azithromycin Dihydrate USP Eq. to Anhydrous Azithromycin	USP	1.314	Active material
2.	Sodium C.M.C (LVP)	BP	0.066	Suspending Agent
3.	Sodium Citrate Anhydrous	BP	0.432	For ph adjustment
4.	Sodium Benzoate	BP	0.0188	Preservative
5.	Sodium Lauryl Sulphate	BP	0.05	Surfactant
6.	Colloidal Silicon Dioxide	BP	0.01	Suspending / Thickening Agent

7.	Pharma Grade Sugar	BP	7.38	Sweetening Agent
8.	Aspartame	BP	0.07	Sweetening Agent
9.	Flavor	IHS	0.06	Flavouring Agent
10.	Sodium Saccharin	BP	0.16	Sweetening Agent
11.	Menthol	BP	0.00178	Soothing agent
12.	Xanthan Gum	BP	0.03	Stabilizing / suspending Agent
13.	Sodium Methylparaben	BP	0.40	Preservatives
Total weight per bottle			**10.00 gm**	

Reference:
BP = British Pharmacopoeia
USP= United State Pharmacopoeia
IHS = In-House
* Quantity to be changed based on potency of API.

3. PHARMACEUTICAL FORM

Oral suspension

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Azithromycin powder for oral suspension is indicated for the treatment of the following infections, when caused by micro-organisms sensitive 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
- Skin and soft tissue infections
- Uncomplicated Chlamydia trachomatis urethritis and cervicitis

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

4.2 Posology and method of administration

Adults

In uncomplicated Chlamydia trachomatis urethritis and cervicitis, the dose is 1,000 mg in one single oral dose.

For all other indications the dose is 1,500 mg, to be administered as 500 mg per day for three consecutive days. Alternatively the same total dose (1,500 mg) can also be given over a period of 5 days with 500 mg on the first day and then 250 mg on days 2 to 5. To treat these patients other pharmaceutical forms are also available.

Elderly people
The same dose as in adult patients is used in the older people. Since older patients can be patients with ongoing proarrhythmic conditions a particular caution is recommended due to the risk of developing cardiac arrhythmia and torsades de pointes.

Children and adolescents (< 18 years)
The total dose in children aged 1 year and older is 30 mg/kg administered as 10 mg/kg once daily for three days, or over a period of five days starting with a single dose of 10 mg/kg on the first day, followed by doses of 5 mg/kg per day for the following 4 days, according to the tables shown below. There are limited data on use in children younger than 1 year.

Weight (kg)	**3-day therapy**	**5-day therapy**		**Contents of the bottle**
	Day 1-3 10 mg/kg/day	**Day 1 10 mg/kg/day**	**Day 2-5 5 mg/kg/day**	
10 kg	2.5 ml	2.5 ml	2.5 ml	15 ml
12 kg	3 ml	3 ml	3 ml	15 ml
14 kg	.5 ml	3.5 ml	1.75 ml	15 ml
16 kg	4 ml	4 ml	2 ml	15 ml
17- 25kg	5 ml	5 ml	2.5 ml	15 ml
26- 35kg	7.5 ml	7.5 ml	3.75 ml	22.5 ml
36- 45kg	10 ml	10 ml	5 ml	30 ml
>45 kg	12.5 ml	12.5 ml	6.25 ml	22.5 ml + 15 ml

OR
As directed by Physician

Method of Administration
Oral use

4.3 Contraindications
Azithromycin is contraindicated in patients with known hypersensitivity to azithromycin, erythromycin or any macrolide antibiotic.

4.4 Special warnings and precautions for use
Hypersensitivity
Serious allergic reactions, including angioedema, anaphylaxis, and dermatologic reactions including Acute Generalized Exanthematous Pustulosis (AGEP), Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported in patients on azithromycin therapy. Fatalities have been reported. Cases of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) have also been reported. Despite initially successful symptomatic treatment of the allergic symptoms, when symptomatic therapy was discontinued, the allergic symptoms recurred soon thereafter 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, hepatitis, cholestatic jaundice, hepatic necrosis, and hepatic failure have been reported, some of which have resulted in death. Discontinue azithromycin immediately if signs and symptoms of hepatitis occur. Infantile hypertrophic pyloric stenosis

Infantile Hypertrophic
Pyloric Stenosis (IHPS) Following the use of azithromycin in neonates (treatment up to 42 days of life), IHPS has been reported. Direct parents and caregivers to contact their physician if vomiting or irritability with feeding occurs

QT Prolongation
Prolonged cardiac repolarization and QT interval, imparting a risk of developing cardiac arrhythmia and torsades de pointes, have been seen with treatment with macrolides, including azithromycin. Cases of torsades de pointes have been spontaneously reported during postmarketting surveillance in patients receiving 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, a history of torsades de pointes, congenital long QT syndrome, bradyarrhythmia or uncompensated heart failure
- Patients on drugs known to prolong the QT interval
- Patients with ongoing proarrhythmic conditions such as uncorrected hypokalemia or hypomagnesaemia, 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.

4.5 Interaction with other medicinal products and other forms of interaction

Azithromyci can interact with the following drugs or groups of drugs:
Antacids, Ergot derivatives, Methylprednisolone, Digoxin and colchicine, Cetirizine, Zidovudine, Cimetidine, Coumarin-Type Oral Anticoagulants:, Nelfinavir etc.

4.6 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 the active substance during pregnancy. Therefore azithromycin should only be used during pregnancy if the benefit outweighs the risk.

Lactation
Azithromycin has been reported to be secreted into human breast milk, but there are no adequate and well-controlled clinical studies in nursing women that have characterized the pharmacokinetics of azithromycin excretion into human 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.

4.7 Effects on ability to drive and use machines
No data are available regarding the influence of azithromycin on a patient's ability to drive or operate machinery.

4.8 Undesirable effects
Blood and lymphatic system disorders: Leukopenia, Neutropenia, Eosinophilia, Thrombocytopenia,, Haemolytic anaemia
Immune system disorders: Angioedema Hypersensitivity, Anaphylactic reaction
Metabolism and nutrition disorders: Anorexia
Psychiatric disorders: Nervousness,Insomnia, Agitation, Aggression, Anxiety, Delirium, Hallucination
Cardiac disorders: Palpitations Torsades de pointes, Arrhythmia, including ventricular tachycardia, Electro-cardiogram QT prolonged

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

5. PHARMACOLOGICAL PROPERTIES

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

Azithromycin is the first of a sub class of macrolide antibiotics known as azalides. The mode of action of azithromycin is inhibition of protein synthesis in bacteria by binding to the 50s ribozomal sub units and preventing translocation of peptides.
Azithromycin demonstrates activity invitro against a wide range of bacteria including;

- Gram-positive Aerobic Bacteria
- Gram-negative Aerobic Bacteria
- Anaerobic bacteria
- Organisms of Sexually transmitted Diseases
- Opportunistic Pathogens Associated with HIV infections

5.2 Pharmacokinetic properties
Absorption
Following oral administration in humans, azithromycin is widely distributed throughout the body; bioavailability is approximately 37%. Administration of azithromycin tablets/suspension following a substantial meal reduces bioavailabilty by at least 50%. The time taken to peak plasma levels is 2-3 hours.
Distribution
In animal studies, high azithromycin concentrations have been observed in phagocytes. In experimental models, higher concentrations of azithromycin are released during active phagocytes that form non-simulated phagocytes. In animal models, this results in high concentration of azithromycin being delivered to the site of infection.
Pharmacokinetic studies in humans have shown markedly higher azithromycin levels in tissues than in plasma (up to 50 times the maximum observed concentration in plasma) indicating that

the drug is heavily tissue bound. Concentrations in target tissues, such as lung, tonsil and prostrate exceed the MIC_{90} for likely pathogens after a single dose of 500mg. **Elimination**
Plasma terminal elimination Half-life closely reflects the tissue depletion half-life of 2 to 4 days. Approximately 12% of an intravenously administered dose is extracted in the urine over 3 days as the parent drug, the majority in the first 24 hours. Biliary excretion of azithromycin is a major route of elimination for unchanged drug following oral administration. Very high concentration of unchanged drug have been found in human bile, together with 10 metabolites, formed by N- and O-demethylation, by hydroxylation of the desosamine and aglycone rings, and by cleavage of the cladinose conjugate. Comparison of HPLC and microbiological assays in tissues suggests that metabolites play no part in the microbiological activity of azithromycin.

5.3 Preclinical safety data
Phospholipidosis (intracellular phospholipid accumulation) has been observed in several tissues (e.g. eye, dorsal root ganglia, liver, gallbladder, kidney, spleen, and/or pancreas) of mice, rats, and dogs given multiple doses of azithromycin. Phospholipidosis has been observed to a similar extent in the tissues of neonatal rats and dogs. The effect has been shown to be reversible after cessation of azithromycin treatment. 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 invivo and in-vitro test models.

Reproductive toxicity:
Teratogenic effects were not observed in rat reproductive toxicity studies. In rats, azithromycin doses of 100 and 200 mg/kg body weight/ 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

Sodium C.M.C (LVP)	BP
Sodium Citrate Anhydrous	BP
Sodium Benzoate	BP
Sodium Lauryl Sulphate	BP
Colloidal Silicon Dioxide	BP
Sucrose	BP
Aspartame	BP
Flavor	IH
Sodium Saccharin	BP

Menthol	BP
Xanthan Gum	BP
Sodium Methyl Paraben	BP

6.2 Incompatibilities
Not Applicable

6.3 Shelf life
24 months

6.4 Special precautions for storage Store
below 30° C. Protect from light.

6.5 Nature and contents of container 1
x 30 ml bottle in a mono-Pack.

6.6 Special precautions for disposal and other handling
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

7. APPLICANT
EXAGON PHARMACEUTICALS LIMITED
Suite No. 502, MKK Plaza, Odumegwu Ojukwu Street,off Abdusalam Abubakar way, Gudu Dist, FCT, Abuja Nigeria.

8. MANUFACTURER
Manufactured by:
HEALTH CARE FORMULATIONS PVT. LTD.
C/8, SARDAR ESTATE, AJWA Road ,
CITY: VADODARA-390019, GUJARAT STATE, INDIA