SUMMARY OF PRODUCT CHARACTERISTICS

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

1 NAME OF THE MEDICINAL PRODUCT:
AZISURE
AZITHROMYCIN ORAL SUSPENSION USP 200 MG/5 ML

COMPOSITION:
Each 5 ml (After Reconsituated) Contains:

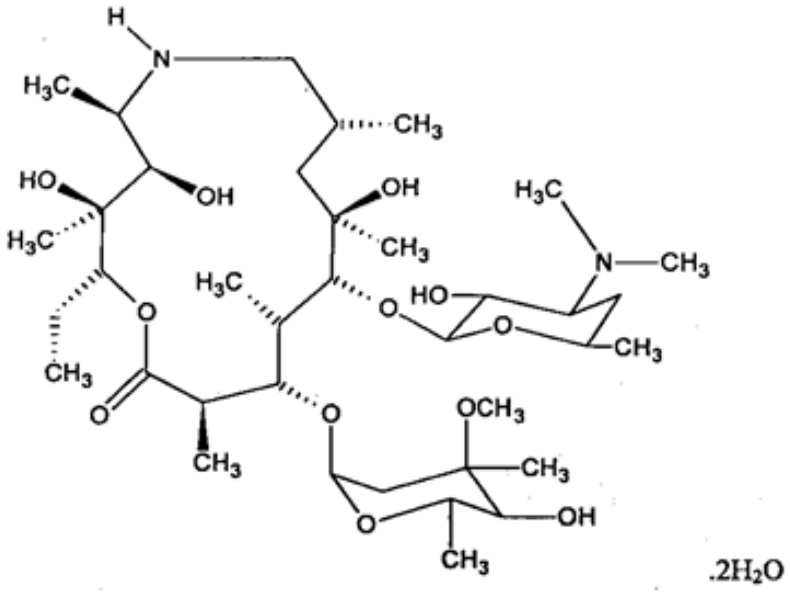
Azithromycin Dihydrate USP	
Eq. to Azithromycin base	200 mg
Flavoured syrup base	q.s.

2 QUALITATIVE AND QUANTITATIVE COMPOSITIONS:

CHEMICAL NAME AND THE STRUCTURAL FORMULA OF EACH ACTIVE INGREDIENT:-
AZITHROMYCIN DIHYDRATE

Chemical Name:
1-oxa-6-azacyclopentadecan-15-one.13-[(2,6-dideoxy-3-C-methyl-3-O-methyl-α-L-ribo-hexapyranosyl) oxy]-2ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-11-[[3,4,6-trideoxy-3-(dimethyl amino)-β-D-xylo-hexapyranosyl] oxy] dihydrate, [2R(2R*,3S*,4R*,5R*, 8R*,10R*,11R*,12S*,13S*,14R*)]

Chemical Structure:



Molecular Formula : $C_{38}H_{72}N_2O_{12.}\ 2H_2O$

Molecular Weight : 785.02 g/mol

NAME AND QUANTITY OF EACH INGREDIENT:

UNIT DOSE

Ingredients	Qty./ 5 ml	Use/Function
Active Ingredient		
Azithromycin Dihydrate eq.to Azithromycin Base USP	200.00	Macrolide Antibacterial Drug
In Active Ingredients		
Sugar BP	2237.00	Sweetening Agent
Sodium Benzoate BP	2.53	Preservative
Aerosil BP	25.00	Stabilizer
Ess. Orange Dry powder speci	27.33	Flavouring Agent
Sodium C.M.C.(MVP) BP	7.40	Stabilizer
Neotame USP	10.00	Sweetening Agent
Citric acid (Anhy) BP	1.67	Preservative
Menthol BP	3.34	Carminative

3 PHARMACEUTICAL FORMS:
Oral suspension

White to off White granular powder after reconstitution given white to off white color suspension with orange flavor

4 CLINICAL PARTICULARS:
4.1 INDICATIONS FOR USE:
Azithromycin is indicated for infection caused by susceptible organisms;

- In lower respiratory tract infections including bronchitis and pneumonia,
- in odontostomatological infections,
- in skin and soft tissue infections,
- in acute otitis media and in upper respiratory tract infections including sinusitis and pharyngitis.
- In sexually transmitted diseases in men and women, azithromycin is indicated in the treatment of uncomplicated genital infections due to *chlamydia trachomatis*. It is also indicated in the treatment of chancroid due to *Haemophilus ducreyi* and uncomplicated genital infection due to non-multiresistance *Neisseria gonorrhea*, concurrent infection with *Trepnema pallidum* should be excluded.
- Azithromycin is indicated, either alone or in combination with rifabutin, for prophylaxis against *mycobacterium avium-intracellulare* complex (MAC) infection, an opportunist infection prevalent in patients with advanced human immune deficiency virus (HIV). Azithromycin is indicated in combination with ethambutol for the treatment of disseminated MAC (DMAC) infection in patients with advanced HIV infection.

4.2 CONTRAINDICATIONS:
Azithromycin is contraindicated in patients with known hypersensitivity to azithromycin, erythromycin or any macrolide antibiotic.

5 SPECIAL PRECAUTIONS FOR USE:
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.

Prolonged cardiac repolarization 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 repolarization.
Prescribing azithromycin in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

6 ADVERSE REACTIONS:
In clinical trials, most of the reported side effects were mild to moderate in severity and were reversible upon discontinuation of the drug. Potentially serious side effects of angioedema and cholestatic jaundice were reported rarely. Approximately 0.7% of the patients (adults and pediatric patients) from the 5-day multiple-dose clinical trials discontinued azithromycin therapy because of treatment-related side effects. In adults given 500 mg/day for 3 days, the discontinuation rate due to treatment-related side effects was 0.6%. In clinical trials in pediatric patients given 30 mg/kg, either as a single dose or over 3 days, discontinuation from the trials due to treatment-related side effects was approximately 1%. Most of the side effects leading to discontinuation were related to the gastrointestinal tract, e.g., nausea, vomiting, diarrhea, or abdominal pain.

Clinical
Adults:
Multiple-dose regimens: Overall, the most common treatment-related side effects in adult patients receiving multiple-dose regimens of azithromycin were related to the gastrointestinal system with diarrhea/loose stools (4-5%), nausea (3%) and abdominal pain (2-3%) being the most frequently reported.
No other treatment-related side effects occurred in patients on the multiple-dose regimens of azithromycin with a frequency greater than 1%. Side effects that occurred with a frequency of 1% or less included the following:
Cardiovascular : Palpitations, chest pain.
Gastrointestinal : Dyspepsia, flatulence, vomiting, melena and cholestatic jaundice.
Genitourinary : Monilia, vaginitis and nephritis.
Nervous System : Dizziness, headache, vertigo and somnolence.
General : Fatigue.
Allergic: Rash, pruritus, photosensitivity and angioedema.

7 USES DURING PREGNANCY, LACTATION:
Pregnancy
There are no adequate data from the use of Azithromycin in pregent 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 use of the active substance during pregnancy. Therefore Azithromycin should only be used during pregnancy if the benefit outweighs the risk.

Lactation
Azithromycin has ben reported to be secreted in to 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.

8 DRUG INTERACTIONS:
Antacids: In a pharmacokinetic study investigating the effects of simultaneous administration of antacid with azithromycin, no effect on overall bioavailability was seen, although peak serum concentrations were reduced by approximately 25%. In patients receiving both azithromycin and antacids, the drugs should not be taken simultaneously.
Cetirizine: In healthy volunteers, co-administration of a 5-day regimen of azithromycin with cetirizine 20 mg at steady-state resulted in no pharmacokinetic interaction and no significant changes in the QT interval.
Didanosine (Dideoxyinosine): Co-administration of 1200 mg/day azithromycin with 400 mg/day didanosine in 6 HIV-positive subjects did not appear to affect the steady-state pharmacokinetics of didanosine as compared with placebo.
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 raised digoxin levels should be borne in mind.

Zidovudine: Single 1000 mg doses and multiple 1200 mg or 600 mg doses of azithromycin had little effect on the plasma pharmacokinetics or urinary 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 the 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.
Ergot 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.
Atorvastatin: Co-administration of atorvastatin (10 mg daily) and azithromycin (500 mg daily) did not alter the plasma concentrations of atorvastatin (based on a HMG CoA-reductase inhibition assay).

9 DOSAGES AND 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.

Older 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	1.25 ml	15 ml
12 kg	3 ml	3 ml	1.5 ml	15 ml
14 kg	3.5 ml	3.5 ml	1.75 ml	15 ml
16 kg	4 ml	4 ml	2 ml	15 ml
17 – 25 kg	5 ml	5 ml	2.5 ml	15 ml
26 – 35 kg	7.5 ml	7.5 ml	3.75 ml	22.5 ml
36 – 45 kg	10 ml	10 ml	5 ml	30 ml
> 45 kg	12.5 ml	12.5 ml	6.25 ml	22.5 ml + 15 ml

The dose for the treatment of pharyngitis caused by *Streptococcus pyogenes* is an exception: in the treatment of pharyngitis caused by *Streptococcus pyogenes* Azithromycin has proved to be effective when it is administered to children as a single dose of 10 mg/kg or 20 mg/kg for 3 days with a maximum daily dose of 500 mg. At these two doses a comparable clinical effect was observed, even if the eradication of the bacteria was more significant at a daily dose of 20 mg/kg.

OR
As directed by Physician

10 OVERDOSAGE:
According to toxicity studies in animals or clinical pharmacology studies performed with supra-therapeutic doses, the most important signs to be expected following acute overdosage of Azithromycin are central nervous system symptoms such as confusion, dizziness, impairment of consciousness, and convulsive seizures, increases in QT interval as well as gastro-intestinal reactions such as nausea and mucosal erosions.

11 PHARMACOLOGY:

Mode of action:
Azithromycin is an azalide, a sub-class of the macrolide 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.

12 PHARMACOKINETICS:
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.

13 STORAGE:
Store below 25°C in a dry place in original package
Do not use later than the date of expiry.
KEEP OUT OF REACH OF CHILDREN.

14 SHELF-LIFE:
24 MONTHS