Azic Oral Suspension
Azithromycin Oral Suspension 200 mg/5 ml

COMPOSITION:
Each 5 ml contains:
Azithromycin Dihydrate USP
eq. to Anhydrous Azithromycin 200 mg
Flavoured Syrup Base q.s.
Colour: Erythrosine

PHARMACODYNAMIC:
General properties
Pharmacotherapeutic group: antibacterials for systemic use; macrolides; azithromycin, ATC code: J01FA10
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.

PHARMACOKINETIC:
Absorption
The biological availability of azithromycin after oral administration is approximately 37%. Peak plasma levels are achieved 2-3 hours after taking the medicinal product.
Distribution
After oral administration, azithromycin is distributed throughout the entire body. Pharmacokinetic studies have shown clearly higher azithromycin levels in the tissues than in the plasma (up to 50 times the maximum observed concentration in plasma). This indicates that the substance is bound in the tissues in considerable quantities.
Concentrations in the infected tissues, such as lungs, tonsil and prostate are higher than the MRC90 of the most frequently occurring pathogens after a single dose of 500 mg.
The protein binding of azithromycin in serum is variable and varies, depending on the serum concentration, from 52% at 0.05 mg/l to 12% at 0.5 mg/l. The steady state distribution volume is 31.1 l/kg.
Elimination
The terminal plasma-elimination half-life closely follows the tissue depletion half-life from 2 to 4 days.
Approximately 12% of an intravenously administered dose of azithromycin is, over a period of 3 days, excreted unchanged in the urine. High concentrations of unchanged azithromycin were found in human bile. In this, ten metabolites were also detected (formed by N- and O- desmethylation, by hydroxylation of the desosamin and aglycon rings and by splitting the cladinose conjugate). A comparison of fluid chromatography and microbiological assessment methods shows that the metabolites are microbiologically inactive.
In animal models high concentrations of azithromycin were found in phagocytes. Also it has been shown that during active phagocytosis higher concentrations of azithromycin are released than during inactive phagocytosis. In animal models this process was shown to contribute to the accumulation of azithromycin in infectious tissue.
Pharmacokinetics in special populations
Renal insufficiency
Following a single oral dose of azithromycin 1 g, mean C_{max} and AUC_{0-120} 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 > 80 ml/min). In subjects with severe renal impairment, the mean C_{max} and AUC_{0-120} increased 61% and 33% 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 have 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 C_{max} achieved is slightly lower than adults with 224 ug/l in children aged 0.6-5 years and after 3 days dosing and 383 ug/l in those aged 6-15 years. The $t_{1/2}$ of 36 h in the older children was within the expected range for adults.

INDICATION:
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.

POSOLOGY AND METHOD OF ADMINISTRATION:
Azic Oral Suspension can be taken with or without food. Shake the bottle well before you use the Suspension.

PEDIATRIC DOSAGE GUIDELINES FOR OTITIS MEDIA, ACUTE BACTERIAL SINUSITIS, AND COMMUNITY-ACQUIRED PNEUMONIA (Age 6 months and above) Based on Body Weight

OTITIS MEDIA AND COMMUNITY-ACQUIRED PNEUMONIA: (5-Day Regimen) *

Dosing Calculated on 10 mg/kg/day Day 1 and 5 mg/kg/day Days 2 to 5.			
Weight	**200 mg/5 mL**		**Total mL per Treatment Course**
(kg)	**Day 1**	**Days 2–5**	
5			7.5 mL
10			15 mL
20	5 mL; (1 tsp)	2.5 mL; (½ tsp)	15 mL
30	7.5 mL; (1½ tsp)	3.75 mL; (¾ tsp)	22.5 mL
40	10 mL; (2 tsp)	5 mL; (1 tsp)	30 mL
50 and above	12.5 mL; (2½ tsp)	6.25 mL; (1¼ tsp)	37.5 mL

*Effectiveness of the 3-day or 1-day regimen in pediatric patients with community-acquired pneumonia has not been established.

OTITIS MEDIA AND ACUTE BACTERIAL SINUSITIS: (3-Day Regimen) *

Dosing Calculated on 10 mg/kg/day.		
Weight	**200 mg/5 mL**	**Total mL per Treatment Course**
(kg)	**Day 1-3**	
5		7.5 mL
10		15 mL
20	5 mL; (1 tsp)	15 mL
30	7.5 mL; (1½ tsp)	22.5 mL
40	10 mL; (2 tsp)	30 mL
50 and above	12.5 mL; (2½ tsp)	37.5 mL

*Effectiveness of the 5-day or 1-day regimen in pediatric patients with acute bacterial sinusitis has not been established.

OTITIS MEDIA: (1-Day Regimen)

Dosing Calculated on 30 mg/kg as a single dose.		
Weight	**200 mg/5 mL**	**Total mL per Treatment Course**
(kg)	**1-Day Regimen**	
5	3.75 mL;(3/4 tsp)	3.75 mL
10	7.5 mL;(1½ tsp)	7.5 mL
20	15 mL;(3 tsp)	15 mL
30	22.5 mL;(4½ tsp)	22.5 mL
40	30 mL;(6 tsp)	30 mL
50 and above	37.5 mL;(7½ tsp)	3.75 mL

PEDIATRIC DOSAGE GUIDELINES FOR PHARYNGITIS/TONSILLITIS (Age 2 years and above, Based on Body Weight)
PHARYNGITIS/TONSILLITIS: (5-Day Regimen)

Dosing Calculated on 12 mg/kg/day for 5 days.		
Weight	**200 mg/5 mL**	**Total mL per Treatment Course**
(kg)	**Day 1**	
8	2.5 mL; (½ tsp)	12.5 mL
17	5 mL; (1 tsp)	25 mL
25	7.5 mL; (1½ tsp)	37.5 mL
33	10 mL; (2 tsp)	50 mL
40	12.5 mL; (2½ tsp)	62.5 mL

SPECIAL WARNING AND PRECAUTION FOR USE:
Hypersensitivity
As with erythromycin and other macrolides, rare serious allergic reactions, including angioneurotic oedema and anaphylaxis (rarely fatal), dermatologic reactions including acute generalised exanthematous pustulosis (AGEP), Stevens Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) (rarely fatal) and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported. Some of these reactions with azithromycin have resulted in recurrent symptoms and required a longer period of observation and treatment.
If an allergic reaction occurs, the medicinal product 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.
Since 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
Cardiovascular Events
Prolonged cardiac repolarization and QT interval, imparting a risk of developing cardiac arrhythmia and torsades de pointes, have been seen in treatment with macrolides including azithromycin
Azithromycin powder for oral suspension is not suitable for treatment of severe infections where a high concentration of the antibiotic in the blood is rapidly needed.

CONTRAINDICATION:
The use of this product is contraindicated in patients with hypersensitivity to azithromycin, erythromycin, any macrolide or ketolide antibiotic, or to any of the excipients.

INTERACTION WITH OTHER MEDICINE AND CONCOMITANT USE:
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 medicinal products should not be taken simultaneously.
Cetirizine
In healthy volunteers, coadministration 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)
Coadministration 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 and colchicine (P-gp substrates)
Concomitant administration of macrolide antibiotics, including azithromycin, with P-glycoprotein substrates such as digoxin and colchicine, has been reported to result in increased serum levels of the P-glycoprotein substrate. Therefore, if azithromycin and P-gp substrates such as digoxin are administered concomitantly, the possibility of elevated serum concentrations of the substrate should be considered.
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
Due to the theoretical possibility of ergotism, the concurrent use of azithromycin with ergot derivatives is not recommended.
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.
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).
Carbamazepine
In a pharmacokinetic interaction study in healthy volunteers, no significant effect was observed on the plasma levels of carbamazepine or its active metabolite in patients receiving concomitant azithromycin.
Nelfinavir
Co-administration of azithromycin (1200 mg) and nelfinavir at steady state (750 mg three times daily) resulted in increased azithromycin concentrations. No clinically significant adverse effects were observed and no dose adjustment is required.
Rifabutin
Co-administration of azithromycin and rifabutin did not affect the serum concentrations of either medicinal product.
Neutropenia was observed in subjects receiving concomitant treatment of azithromycin and rifabutin. Although neutropenia has been associated with the use of rifabutin, a causal relationship to combination with azithromycin has not been established.
Sildenafil
In normal healthy male volunteers, there was no evidence of an effect of azithromycin (500 mg daily for 3 days) on the AUC and C_{max} of sildenafil or its major circulating metabolite.
Terfenadine
Pharmacokinetic studies have reported no evidence of an interaction between azithromycin and terfenadine. There have been rare cases reported where the possibility of such an interaction could not be entirely excluded; however there was no specific evidence that such an interaction had occurred.
Theophylline
There is no evidence of a clinically significant pharmacokinetic interaction when azithromycin and theophylline are co-administered to healthy volunteers.
Triazolam
Co-administration of azithromycin 500 mg on Day 1 and 250 mg on Day 2 with 0.125 mg triazolam on Day 2 had no significant effect on any of the pharmacokinetic variables for triazolam compared to triazolam and placebo.
Trimethoprim/sulfamethoxazole
Co-administration of trimethoprim/sulfamethoxazole (160 mg/800 mg) for 7 days with azithromycin 1200 mg on Day 7 had no significant effect on peak concentrations, total exposure or urinary excretion of either trimethoprim or sulfamethoxazole. Azithromycin serum concentrations were similar to those seen in other studies.
Substances that prolong the QT interval
Azithromycin should not be used concomitantly with other active substances that prolong the QT interval

PREGNACY 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.
Breastfeeding
Azithromycin has been reported to be secreted into human breast milk, but there are no adequate and well-controlled clinical studies in breastfeeding women that have characterized the pharmacokinetics of azithromycin excretion into human breast milk.
Fertility
In fertility studies conducted in rat, reduced pregnancy rates were noted following administration of azithromycin. The relevance of this finding to humans is unknown.

ADVERSE REACTION:
Commonly reported side effects of azithromycin include:
- Diarrhoea
- Abdominal pain
- Difficult or painful urination
- Vomiting
- Fever
- Acid or sour stomach
- Aggression or anger
- Excessive air or gas in stomach
- Heartburn
- Dry or scaly skin
- Dizziness
- Drowsiness

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
There is no evidence to suggest that azithromycin may have an effect on a patient's ability to drive or operate machinery. Visual impairment and vision blurred may have an effect on a patient's ability to drive or operate machinery.

OVERDOSE:
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.

INCOMPATIBILITY:
Not applicable

SHELF LIFE:
3 years

PACKAGING:
30 ml HDPE bottle packed in a carton along with pack insert and two sided spoon.

STORAGE CONDITION:
Store in dry place below 30^0C. Protect from light & moisture.
Keep medicine out of reach of children.

Product of

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