Zynomax

A. Tablet 250mg
Azithromycin 250mg

B. Powder for Oral Suspension 200mg/5ml
Azithromycin 200mg/5ml

CLINICAL PHARMACOLOGY

Pharmacodynamic Properties

Pharmacotherapeutic group: Macrolides, ATC code J01FA.

Azithromycin is the first of a subclass of macrolide antibiotics, known as azalides, and is chemically different from erythromycin. Chemically it is derived by insertion of a nitrogen atom into 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.

Azithromycin binds to the 23S rRNA of the 50S ribosomal subunit. It blocks protein synthesis by inhibiting the transpeptidation/translocation step of protein synthesis and by inhibiting the assembly of the 50S ribosomal subunit.

Antibacterial spectrum

The susceptibility of bacterial species to azithromycin is shown below.

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.
In-vitro susceptibility data do not always correlate with clinical results.

Organisms that are commonly susceptible to azithromycin include:

Aerobic and facultative gram-positive bacteria (erythromycin-susceptible isolates): *S. aureus, Streptococcus agalactiae,* S. pneumoniae,* Streptococcus pyogenes,** other b-hemolytic streptococci (Groups C, F, G) and viridans streptococci. Macrolide-resistant isolates are encountered relatively frequently among aerobic and facultative gram-positive bacteria, in particular among methicillin-resistant *S. aureus* (MRSA) and penicillin-resistant *S. pneumoniae* (PRSP).

Aerobic and facultative gram-negative bacteria: *Bordetella pertussis, Haemophilus ducreyi,* Haemophilus influenzae,* Haemophilus parainfluenzae,* Legionella pneumophila, Moraxella catarrhalis,** and *Neisseria gonorrhoeae.* Pseudomonas* spp. and most *Enterobacteriaceae* are inherently resistant to azithromycin, although azithromycin has been used to treat *Salmonella enterica* infections.

Anaerobes: *Clostridium perfringens*, *Peptostreptococcus* spp. and *Prevotella bivia.*

Other bacterial species: *Borrelia burgdorferi, Chlamydia trachomatis, Chlamydophila pneumoniae,* Mycoplasma pneumoniae,* Treponema pallidum, and Ureaplasma urealyticum.*

Opportunistic pathogens associated with HIV infection: Eukaryotic microorganisms *Pneumocystis jirovecii* and *Toxoplasma gondii.*

* The efficacy of azithromycin against the indicated species has been demonstrated in clinical trials.

Pharmacokinetic Properties

Absorption

Following oral administration in humans, azithromycin is widely distributed throughout the body; bioavailability is approximately 37%. 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 phagocytosis than from non-stimulated phagocytes.

In animal models this results in high concentrations of azithromycin being delivered to the site of infection. Pharmacokinetic studies in humans have shown markedly higher azithromycin levels in tissue 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 prostate exceed the MIC90 for likely pathogens after a single dose of 500 mg.

Following oral administration of daily doses of 600 mg azithromycin, mean maximum plasma concentration (C max) was 0.33 µg/ml and 0.55 µg/ml at Day 1 and Day 22 respectively.

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 excreted 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 concentrations 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.

Pharmacokinetics in Special Patient Groups

Elderly

In elderly volunteers (>65 years), slightly higher AUC values were seen after a 5-day regimen than in young volunteers (<40 years), but these are not considered clinically significant, and hence no dose adjustment is recommended.

Renal Impairment

The pharmacokinetics of azithromycin in subjects with mild to moderate renal impairment were not affected following a single one gram dose of immediate release azithromycin. Statistically significant differences in AUC_{0-120}, C_{max} and CLr were observed between the group with severe renal impairment and the group with normal renal function.

Hepatic Impairment

In patients with mild (Class A) to moderate (Class B) hepatic impairment there is no evidence of a marked change in serum pharmacokinetics of azithromycin compared to those with normal hepatic function. In these patients urinary clearance of azithromycin appears to increase, perhaps to compensate for reduced hepatic clearance.

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 significance of the finding for animals and humans is unknown.

I. INDICATIONS

Zynomax is indicated for infections caused by susceptible organisms; in lower respiratory tract infections including bronchitis and pneumonia, in skin and soft tissue infections, in acute otitis media and in upper respiratory tract infections including sinusitis and pharyngitis/tonsillitis. (Penicillin is the usual drug of choice in the treatment of Streptococcus pyogenes pharyngitis, including the prophylaxis of rheumatic fever. Zynomax is generally effective in the eradication of streptococci from the oropharynx, however, data establishing the efficacy of Zynomax and the subsequent prevention of rheumatic fever are not available at present.)

In sexually transmitted diseases in men and women, Zynomax 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- multiresistant Neisseria gonorrhoea; concurrent infection with Treponema pallidum should be excluded.

II.DOSAGE AND ADMINISTRATION

Oral Zynomax should be administered as a single daily dose. The period of dosing with regard to infection is given below. Zynomax can be taken with or without food.

In Adults:

For the treatment of sexually transmitted disease caused by *Chlamydia trachomatis*, or non-multiresistant *Neisseria gonorrhea*, the dose is 1000 mg as a single oral dose.

For all other indications in which the oral formulation is administered, the total dosage of 1500 mg should be given as 500 mg daily for 3 days. As an alternative, the same total dose can be given 5 days with 500 mg given on day 1, then 250 mg daily on days 2 to 5.

In Children:

The maximum recommended total dose for any treatment is 1500 mg for children.
In general, the total dose in children is 30 mg/kg. Treatment for pediatric streptococcal pharyngitis should be dosed at a different regimen (see below).
The total dose 30 mg/kg should be given as single daily dose of 10 mg/kg daily for 3 day, or given over 5 days with a single daily dose of 10 mg/kg on day 1, then 5 mg/kg on days 2-5.
As an alternative to the above dosing, treatment for children with acute otitis media can be given as a single dose of 30 mg/kg.

For pediatric streptococcal pharyngitis, azithromycin given as a single dose of 10 mg/kg or 20 mg/kg for 3 days has been shown to be effective; however, a daily dose of 500 mg must not be exceeded. In clinical trials comparing these two dosage regimens, similar clinical efficacy was observed but greater bacteriologic eradication was evident at the 20 mg/kg/day dose. However, penicillin is the usual drug of choice for the treatment of *Streptococcus pyogenes* pharyngitis, including prophylaxis of rheumatic fever.

For children weighing less than 15 kg, Zynomax should be measured as closely as possible. For children weighing 15 kg or more, Zynomax should be administered according to the guide provided below:

ZYNOMAX POWDER FOR ORAL SUSPENSION 30mg/kg
Total Treatment Dose

Weight (kg)	3-Day Regimen	5-Day Regimen
< 15	10 mg/kg once daily on days 1-3	10 mg/kg on day 1,then 5 mg/kg once daily on days 2 - 5
15-25	200 mg (5 ml) once daily on days 1 - 3	200 mg (5 ml) on day 1, then 100mg (2.5 ml) once daily on days 2-5
26-35	300 mg (7.5 ml) once daily on days 1 - 3	300 mg (7.5 ml) on day 1, then 150mg (3.75 ml) once daily on days 2-5
36-45	400 mg (10 ml) once daily on days 1 - 3	400 mg (10 ml) on day 1, then 200mg (5 ml) once daily on days 2-5
>45	Dose as per adults.	Dose as per adults.

Zynomax tablets should only be administered to children weighing more than 45kg.

Special populations:

Elderly:

The same dosage as in adult patients is used in the elderly. Elderly patients may be more susceptible to the development of torsades de pointes arrhythmia than younger patients

Patients with Renal Impairment:

No dose adjustment is necessary in patients with mild to moderate renal impairment (GFR 10 – 80 ml/min). Caution should be exercised when azithromycin is administered to patients with severe renal impairment (GFR < 10 ml/min)

Patients with Hepatic Impairment

The same dosage as in patients with normal hepatic function may used in patients with mild to moderate hepatic impairment.

III. CONTRAINDICATIONS

The use of azithromycin is contraindicated in patients with hypersensitivity to azithromycin, erythromycin, any macrolide or ketolide antibiotic, or to any excipient used in the product.

IV. WARNING AND PRECAUTIONS

Hypersensitivity

As with erythromycin and other macrolides, rare serious allergic reactions, including angioedema and anaphylaxis (rarely fatal), dermatologic reactions including Steven-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 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.

Hepatotoxicity

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.

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 (IHPS)

Following the use of azithromycin in neonates (treatment up to 42 days of life), infantile hypertrophic pyloric stenosis (IHPS) has been reported. Parents and caregivers should be informed to contact their physician if vomiting or irritability with feeding occurs.

Ergot derivatives

In patients receiving ergot derivatives, ergotism has been precipitated by coadministration of some macrolide antibiotics. There are no data concerning the possibility of an interaction between ergot and azithromycin. However, because of the theoretical possibility of ergotism, azithromycin and ergot derivatives should not be coadministered.

Superinfection

As with any antibiotic preparation, observation for signs of superinfection with non-susceptible organisms, including fungi is recommended.

Clostridium difficile-associated diarrhea

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including azithromycin, and may range in severity from mild diarrhea 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 present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

Renal impairment

In patients with severe renal impairment (GFR <10 ml/min) a 33% increase in systemic exposure to azithromycin was observed.

Prolongation of the QT Interval

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. Prescribers should consider the risk of QT prolongation, which can be fatal, when weighing the risks and benefits of Zynomax for at-risk groups including:

- Patients with congenital or documented QT prolongation
- Patients currently receiving treatment with other active substances known to prolong QT interval, such as antiarrhythmics of Classes IA and III, antipsychotic agents, antidepressants, and fluoroquinolones.
- Patients with electrolyte disturbance, particularly in cases of hypokalemia and hypomagnesemia.
- Patients with clinically relevant bradycardia, cardiac arrhythmia or cardiac insufficiency.
- Elderly patients: elderly patients may be more susceptible to drug-associated effects on the QT interval.

QTc interval prolongation was studied in a randomized, placebo-controlled parallel trial in 116 healthy subjects who received either hloroquine (1000 mg) alone or in combination with azithromycin (500 mg, 1000 mg, and 1500 mg once daily). Co-administration of azithromycin increased the QTc interval in a dose- and concentration-dependent manner. In comparison to chloroquine alone, the maximum mean (95% upper confidence bound) increases in QTcF were 5 (10) ms, 7 (12) ms and 9 (14) ms with the co-administration of 500 mg, 1000 mg and 1500 mg azithromycin, respectively.

Myasthenia gravis

Exacerbations of the symptoms of myasthenia gravis have been reported in patients receiving azithromycin therapy.

Effects on Ability to Drive and Use Machines

There is no evidence to suggest that azithromycin may have an effect on the patient's ability to drive or operate machinery.

In the event of severe acute hypersensitivity reactions, such as anaphylaxis, severe cutaneous adverse reactions (SCARs) [e.g. Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) & acute generalised exanthematous pustulosis (AGEP)], azithromycin should be discontinued immediately and appropriate treatment should be urgently initiated.

Zynomax Powder for Oral Suspension: Contains aspartame, unsuitable for phenylketonurics

V. PREGNANCY, LACTATION AND FERTILITY

Pregnancy

Animal reproduction studies have been performed at doses up to moderately maternally toxic dose concentrations. In these studies, no evidence of harm to the fetus due to azithromycin was found. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, azithromycin should be used during pregnancy only if clearly needed.

Lactation

Limited information available from published literature indicates that azithromycin is present in human milk at an estimated highest median daily dose of 0.1 to 0.7 mg/kg/day. No serious adverse effects of azithromycin on the breast-fed infants were observed.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from azithromycin therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility
In fertility studies conducted in rats, reduced pregnancy rates were noted following administration of azithromycin. The relevance of this finding to humans is unknown.

VI. 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 24%. In patients receiving both oral 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 charges in the QT interval.

Didanosine (Dideoxyinosine): Co-administration of 1200 mg/day azithromycin with 400 mg/day didanosine in six HIV-positive subjects did not appear to affect the steady-state pharmacokinetics of didanosine as compared to placebo.

Digoxin and colchicine: 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-glycoprotein substrates such as digoxin are administered concomitantly, the possibility of elevated serum digoxin concentrations should be considered. Clinical monitoring, and possibly serum digoxin levels, during treatment with azithromycin and after its discontinuation are necessary.

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.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.

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

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

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). However, post-marketing cases of rhabdomyolysis in patients receiving azithromycin with statins have been reported.

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.

Cimetidine: In a pharmacokinetic study investigating the effects of a single dose of cimetidine, given 2 hours before azithromycin ,on the pharmacokinetic of azithromycin, no alteration of azithromycin pharmacokinetics was seen.

Coumarin-Type Oral Anticoagulants: In a pharmacokinetic interaction study, azithromycin did not alter the anticoagulant effect of a single dose of 15-mg 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 who 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 coadministration of these drugs is necessary, cyclosporin levels should be monitored and the dose adjusted accordingly.

Efavirenz: Co-administration of a single dose of 600 mg azithromycin and 400 mg efavirenz daily for 7 days did not result in any clinically significant pharmacokinetic interactions.

Fluconazole: Coadministration 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 coadministration of fluconazole.

Indinavir: Coadministration of a single dose of 1200 mg azithromycin had no statistically significant effect on the pharmacokinetics of indinavir administered as 800 mg three times daily for 5 days.

Methylprednisolone: In a pharmacokinetic interaction study in healthy volunteers, azithromycin had no significant effect on the pharmacokinetics of methylprednisolone.

Midazolam: In healthy volunteers, co-administration of 500 mg/day azithromycin for 3 days did not cause clinically significant changes in the pharmacokinetics and pharmacodynamics of a single 15 mg dose of midazolam.

Nelfinavir: Coadministration 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 was required.

Rifabutin: Coadministration of azithromycin and rifabutin did not affect the serum concentrations of either drug. Neutropenia is seen when taken with rifabutin. Although neutropenia has been associated with the use of rifabutin, a causal relationship to combination with azithromycin has not been established.

Sildenafil: No evidence of an effect of azithromycin (500mg daily for 3 days) on the AUC and Cmax, of sildenafil or its major circulating metabolite.

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.

Triazolam: In 14 healthy volunteers, co-administration of 500 mg azithromycin 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.

Theophylline: There is no evidence of an interaction when azithromycin and theophylline are co-administered.

Trimethoprim/ Sulfamethoxazole: Co-administration of trimethoprim/sulfamethoxazole DS (160 mg/800 mg) for 7 days with 1200 mg azithromycin 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.

VII. SIDE EFFECTS
Azithromycin is well tolerated with a low incidence of side effects.

The following undesirable effects have been reported:

Blood and Lymphatic System Disorders
Transient episodes of mild neutropenia, thrombocytopenia.

Ear and Labyrinth Disorders
Hearing impairment (including hearing loss, deafness and/or tinnitus), vertigo.

Gastrointestinal Disorders
Nausea, vomiting/diarrhea (rarely resulting in dehydration), loose stools, abdominal discomfort (pain/cramps), and flatulence, dyspepsia, constipation, pseudomembranous colitis, pancreatitis, and rare reports of tongue discoloration, infantile hypertrophic pyloric stenosis.

Hepatobiliary Disorders
Abnormal liver function, hepatitis and cholestatic jaundice have been reported, as well as rare cases of hepatic necrosis and hepatic failure, which have rarely resulted in death. However, a causal relationship has not been established.

Skin and Subcutaneous Tissue Disorders
Allergic reactions including pruritus, rash, photosensitivity, edema, urticaria, and angioedema. Rarely, serious skin reactions including erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis and DRESS have been reported. Frequency not known: severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) & acute generalised exanthematous pustulosis (AGEP).

General Disorders and Administration Site Conditions
Local pain and inflammation at the site of infusion, asthenia has been reported, although a causal relationship has not been established; fatigue, and malaise.

Infections and Infestations
Moniliasis and vaginitis.

Immune System Disorders
Anaphylaxis (rarely fatal).

Metabolism and Nutrition Disorders
Anorexia.

Psychiatric Disorders
Aggressive reaction, nervousness, agitation, and anxiety.

Nervous System Disorders
Dizziness, convulsions (as seen with other macrolides), headache, hyperactivity, hypoesthesia, paresthesia, somnolence, and syncope. There have been rare reports of taste/smell perversion and/or loss. However, a causal relationship has not been established.

Cardiac Disorders
Palpitations and arrhythmias including ventricular tachycardia (as seen with other macrolides) have been reported. There have been rare reports of QT prolongation and torsades de pointes. A causal relationship between azithromycin and these effects has not been established.

Vascular Disorders
Hypotension

Musculoskeletal and Connective Tissue Disorders
Arthralgia.

Renal and Urinary Disorders
Interstitial nephritis and acute renal failure.

X. 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.

XI. APPEARANCE
Zynomax Tablet 250mg
Zynomax tablet appearance is white, capsule shaped, film coated tablets plain on both sides.
Each film-coated tablet contains Azithromycin Dihydrate equivalent to Azithromycin 250mg. Other ingredients include Sodium Lauryl Sulphate, Croscarmellose Sodium, Pregelatinized Starch, Magnesium Stearate, Dicalcium Phosphate, Purified Water. The film-coating contains Lactose Monohydrate, Hypromellose, Titanium Dioxide and Triacetin.

Zynomax Powder for Oral Suspension 200mg/5ml
Zynomax powder for oral suspension is presented as a white to off white homogenous granules; on reconstitution with water, white to off white with tutty fruity flavoured homogenous suspension containing the equivalent of 200 mg Azithromycin per 5 ml.
Other ingredients include Icing Sugar, Aspartame, Xanthan Gum, Povidone 30, Trisodium Phosphate Anhydrous and Tutti Fruity Flavour.

XII. SHELF LIFE
Refer to carton for shelf life.
For dry powder, the reconstituted suspension form lasts up to 5 days.

XIII. STORAGE CONDITION
Zynomax Tablet 250mg
Store below 30°C.

Zynomax Powder for Oral Suspension 200mg/5ml
Store below 30°C for both dry powder and reconstituted suspension.

Protect from light and moisture.
Keep out of reach of children.
Jauhi daripada kanak-kanak.

XIX. AVAILABILITY
The powder for oral suspension is packed in high density polyethylene bottles of 15ml and 20ml.
The film-coated tablets are packed of 1 x 6's, 1 x 10's, 3 x 10's, 9 x 10's and 10 x 10's in PVC/PVDC blisters.
Not all pack sizes and presentation are available locally.

XV. INSTRUCTION FOR USE AND HANDLING, AND DISPOSAL
Powder for Oral Suspension 200mg/5ml for 20ml
Tap the bottle to loosen the powder.
Add 9ml of water and shake well.
Shake immediately prior to use.
For children weighing less than 15 kg, the suspension should be measured as closely as possible. For children weighing 15 kg or more, the suspension should be administered using an appropriate measuring device.

Powder for Oral Suspension 200mg/5ml for 15ml
Tap the bottle to loosen the powder.
Add 7ml of water and shake well.
Shake immediately prior to use.
For children weighing less than 15 kg, the suspension should be measured as closely as possible. For children weighing 15 kg or more, the suspension should be administered using an appropriate measuring device.

XVI. PRODUCT REGISTRATION HOLDER
PRODUCT REGISTRATION HOLDER (MALAYSIA):
Duopharma Marketing Sdn. Bhd.
Lot No. 2, 4, 6, 8, & 10, Jalan P/7, Section 13, Bangi Industrial Estate,
43650 Bandar Baru Bangi, Selangor, Malaysia.

PRODUCT REGISTRATION HOLDER (SINGAPORE):
Duopharma (Singapore) Pte. Ltd.
25, International Business Park,
#03-53 German Centre,
Singapore 609916

XVII. MANUFACTURER
Duopharma Manufacturing (Bangi) Sdn. Bhd.
Lot No. 2 & 4, Jalan P/7, Section 13,
Bangi Industrial Estate, 43650 Bandar Baru Bangi,
Selangor, Malaysia.

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