Azithronext™

Azithromycin

250mg Capsules , 250mg & 500mg Film Coated Tablets

COMPOSITION

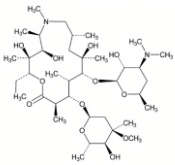
AZITHRONEXT 250mg Capsules: Each capsule contains:
Azithromycin as dihydrate.....250mg.
(BP Specification)

AZITHRONEXT 250mg Tablets: Each film coated tablet contains:
Azithromycin (as dihydrate) .... 250mg.
(USP Specifications)

AZITHRONEXT 500mg Tablets: Each film coated tablet contains:
Azithromycin (as dihydrate) .... 500mg.
(USP Specifications)

DESCRIPTION

AZITHRONEXT (Azithromycin) is nitrogen containing macrolide or azalide for oral administration. Chemically azithromycin is (2R, 3S, 4R 5R, 8R, 10R, 11R, 12S, 13S, 14R)-13-[(2,6-dideoxy-3-C-methyl-3-O-methyl-a-L-ribohexopyranosyl) oxy]-2-ethyl-3,4,10-trihydroxy- 3,5,6,8,10,12,14-hepta methyl-11[(3,4,6-trideoxy-3-(dimethylamino)- β-D-xylo-hexopyranosyl] oxy]-1-oxa-6-azacyclopenta decan-15- one. The molecular formula is $C_{38}H_{72}N_2O_{12}$ and the structural formula is:



CLINICAL PHARMACOLOGY

Mechanism of Action:

Azithromycin exerts its antibacterial action by binding to the 50s ribosomal subunit of susceptible organisms and thus interfering with microbial protein synthesis and inhibition, of peptide translocation. Nucleic acid synthesis is not effected.

Pharmacokinetics:

Following oral administration about 40% of the dose of azithromycin is bioavailable. Absorption from the capsule formulation is reduced by food but there is no significant effect on the bioavailability of tablet formulation even after a high fat meal. Peak plasma concentrations are achieved 2 to 3 hours after a dose but azithromycin Is extensively distributed to the tissues and tissue concentration subsequently remain much higher than those In blood. High concentrations are taken up into white blood cells. Small amount of azithromycin are demethylated In liver and it Is excreted in bile as unchanged drug and metabolites. About 20% of the amount In the systemic circulation is excreted In the urine. The terminal elimination half-life is probably in excess 0(40 hours.

Special Populations:

Renal Insufficiency:

Following a single dose of azithromycin 1g orally, the pharmacokinetics in subjects with mild to moderate renal impairment IGFR 10- (30mLfinin) were not effected. Significant differences in AUG and CID were observed between subjects with severe renal impairment (GFR < l0mL/ min) and subjects with normal renal function.

Hepatic Insufficiency:

in patents with mild (Class A) to moderate (Class 01 hepatic impairment, there is no evidence of a marked change in serum pharmacokinetics of azithromycin compared to those with normal hepatic function.

Microbiology:

Azithromycin has been shown to be active against most Isolates of Me following micro-organisms, both in vitro and in clinical Infections.

Aerobic and facultative gram-positive organisms:

Streptococcus pneumoniae, penicillin-resistant, penicillin intermediate, Streptococcus pyogenes, Staphylococcus aureus, Streptococcus agalactiae, Streptococci (Groups C, E Gl Widens group streptococci, Corynebacterium diptheriae. Azithromycin demonstrates cross-resistance with erythromycin-resistant Gram positive strains, including Streptococcus faecalis (entrococcus) and most strains of methicillin-resistant staphylococci.

Aerobic and facultative gram-negative organisms:

Haemophilus ducreyi, Haemophilus influenzae, Moraxella catarrhalis, Neisseria gonorrhoeae, Bordetella pertussis, Legionella pneumophila, Haemophilus parainfluenzae, Acinetobacter species, Yersinia species, Shigella species, Pasteurella species, Vibrio cholerae and Parahaemolyticus, Plesiomonas shigelloides.

Anaerobic-micro-organisms:

Peptostreptococcus species, Prevotella bivia, Bacteroides fragilis and Bacteroides species, Clostridium perfringens, Peptococcus species, Fusobacteriurn necrophorum and Propianibacterium acnes.

Others:

Chlamydia pneumoniae, Chlamydia trachomatis, Mycoplasma pneumoniae, Ureaplasma urealyticum, Escherichia call, Salmonella, Shigella spp., Mycobacterium avium, Mycobacterium Intracellulare, Toxoplasma gondii, Plasmodium falciparum.

THERAPEUTIC INDICATIONS

AZITHRONEXT (Azithromycin) is indicated for the treatment of patients with mild to moderate infections caused by susceptible strains of the designated micro-organisms in the specific -conditions listed below:

- Lower respiratory tract infections (acute bacterial bronchitis and community acquired pneumonia in patients suitable for outpatient oral treatment and in patients who require initial intravenous therapy).
- Upper respiratory tract Infections (acute sinusitis, acute streptococcal pharyngitis/tonsillitis and acute odds media In children).
- Uncomplicated skin and skin structure infections.
- Sexually transmitted diseases (uncomplicated urethritis and cervicitis). Antimicrobial agents used in high doses for short periods of times to treat non-gonococcal urethritis may mask or delay the symptoms of incubating gonorrhea or syphilis. All patients with sexually-transmitted urethritis or cervicitis should have a serologic test for syphilis and appropriate cultures for gonorrhea performed at the time of diagnosis. Appropriate antimicrobial therapy and follow-up tests for these diseases should be initiated if infection is confirmed.
- Pelvic inflammatory disease in patients who require Initial intravenous therapy.
- Chlamydia trachomatis conjunctivitis and trachoma in adults and in children 12 months or older.
- Prophylaxis and treatment of disseminated mycobacterium avium complex (MAC) disease in adults and children aged more than 12 years.

DOSAGE ANIADMINISTRATION

AZITHRONEXT (Azithromycin) tablets can be taken with or without food.

Adults:

For all indications except for those given below, the usual adult dose of **AZITHRONEXT** (Azithromycin) is 500mg as a single dose daily for 3 days. Alternatively, an initial dose of 500mg may be followed by 250mg daily for a further 4 days.

Sexually transmitted uncomplicated urethritis and cervicitis, 1g as a single dose. Conjunctivitis and trachoma due to chlamydia trachomatis 1g either as a single dose or once weekly for upto 3 weeks. *Treatment of community acquired pneumonia following IV therapy* 500mg as a single daily dose to complete a 7 to 10 day course of therapy. Treatment of pelvic inflammatory disease following IV therapy. 250mg as a single daily dose to complete a 7 day course of therapy. *Prevention of disseminated Mycobacterium avium complex (MAC) disease in adults with HIV infection* 1200mg taken as a single dose once weekly, either alone, or in combination with rifabutin, at its recommended dosage. *Treatment of disseminated Mycobacterium avium complex (MAC) disease in adults with HIV infection* **AZITHRONEXT** (Azithromycin) should be taken at a daily dose of 600mg, in combination with ethambutol at the recommended daily dose of 15mg/kg.

ADVERSE REACTIONS

Very Common:

Diarrhea, abdominal pain, nausea and flatulence.

Common:

Lymphocyte count decreased, eosinophil count increased, anorexia, dizziness, headache, paraesthesia, dysgeusia, deafness, vomiting, dyspepsia, rash, pruritus, arthralgia, fatigue and blood bicarbonate decreased.

Uncommon:

Candidiasis, oral candidiasis, vaginal infection, leukopenia, neutropenia, angioedema, hypersensitivity, nervousness, hypoaesthesia, somnolence, insomnia, hearing impaired, tinnitus, palpitations, gastritis, constipation, hepatitis, aspartate aminotransferase increased, alanine aminotransferase increased, blood bilirubine increased, Steven-Johnson syndrome, photosensitivity reaction, urticaria, blood urea increased, chest pain, oedema, malaise, asthenia and blood potassium abnormal.

Rare:

Thrombocytopenia, hemolytic anemia, agitation, depersonalisation, vertigo, hepatic function abnormal, renal failure acute and nephritis interstitial.

CONTRAINDICATIONS

Azithromycin is contraindicated:

- In patients with known hypersensitivity to azithromycin, erythromycin, any macrolide or ketolide antibiotics.
- In patients with a history of cholestatic jaundice/hepatic dysfunction associated with prior use of azithromycin.
- To use concurrently with ergot derivatives.

PRECAUTIONS

- Azithromycin should not be used in patients with pneumonia who are judged to be inappropriate for oral therapy because of risk factors such as:
- Patients with cystic fibrosis.
- Patients with nosocomially acquired infections.
- Patients with known or suspected bacteremia.
- Patients requiring hospitalization.
- Elderly or debilitated patients.
- Patients with significant underlying health problems that may compromise their ability to respond to their illness (including immunedeficiency or functional asplenia).
- No dose adjustment is needed in patients with mild or moderate renal impairment.
- Caution should be exercised when azithromycin is administered to patients with severe renal impairment (GER< 10mL/min).
- Since azithromycin is metabolized in the liver and excreted in the bile, the drug should not be given to patients suffering from severe liver disease.
- As with any antibiotic preparation, observation for signs of superinfection with non-susceptible organisms Including fungi, is recommended.
- Ventricular arrythmias associated with prolonged QT interval, including ventricular tachycardia and torsades de pointes have been reported with macrolide products. Azithromycin should be used with caution in patients predisposed to QT interval prolongation or in patients taking other medications known to prolong the QT interval.
- 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. If CDAD As suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued.

Pregnancy:

There are no adequate and well-controlled studies in pregnant women. Therefore, azithromycin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers:

It is not known whether azithromycin is excreted into human milk. Azithromycin should only be used in lactating women where adequate alternatives are not available.

Drug Interactions:

Antacids:

In patients receiving both azithromycin and antacids, the drugs should not be taken simultaneously. Azithromycin should be taken at least 1 hour before or 2 hours after the antacid.

Cyclosporine:

Caution should be exercised before considering concurrent administration of these drugs. If co-administration of these drugs is necessary, cyclosporine levels should be monitored and the dose adjusted accordingly.

Theophylline:

Theophylline levels maybe increased in patients taking azithromycin.

Coumarin-type oral anticoagulants:

Consideration should be given to the frequency of monitoring prothrombin time, when azithromycin is used in patients receiving coumarin-type oral anticoagulants.

Digoxin:
In patients receiving concomitant azithromycin, a related azalide Antibiotic and digoxin, the possibility of raised digoxin levels should be borne in mind.

OVERDOSE
Adverse events experienced in higher than recommended doses were similar to those seen at normal doses. The typical symptoms of an overdose with macrolide antibiotics include reversible loss of hearing, severe nausea, vomiting and diarrhea. In the event of overdose, the administration of medicinal charcoal and general symptomatic treatment and supportive measures are indicated as required.

STORAGE
AZITHRONEXT 250mg Capsules:
Store below 30°C. Protect from light and moisture.
AZITHRONEXT 250mg Tablets:
Store at 20°C-25°C. Protect from light and moisture.
(Excursions permitted 15°C to 30°C)
AZITHRONEXT 500mg Tablets:
Store at 20°C-25°C. Protect from light and moisture.
(Excursions permitted 15°C to 30°C)

HOW SUPPLIED
AZITHRONEXT 250mg Capsules: Pack of 10 capsules.
AZITHRONEXT 250mg Tablets: Pack of 6 film coated tablets.
AZITHRONEXT 500mg Tablets: Pack of 6 film coated tablets.

TO BE SOLD AND USED ON THE PRESCRIPTION OF A REGISTERED MEDICAL PRACTITIONER ONLY. KEEP ALL MEDICINES OUT OF THE REACH OF CHILDREN. PLEASE READ THE CONTENTS CAREFULLY BEFORE USE. THIS PACKAGE INSERT IS CONTINUALLY UPDATED FROM TIME TO TIME.

Lactose and Gluten Free

ایزتھرونیکسٹ

(ایزتھرومائسین)

250 ملی گرام کیپسولز

250 ملی گرام اور 500 ملی گرام فلم کوٹڈ گولیاں

خوراک وہدایات:
ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔
صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت کی جائے۔
تمام ادویات بچوں کی پہنچ سے دور رکھیں۔

ایزتھرونیکسٹ

250 ملی گرام کیپسولز

دوا کو 30°C سے کم درجہ حرارت پر، نمی اور روشنی سے محفوظ رکھیں۔

ایزتھرونیکسٹ

250 ملی گرام اور 500 ملی گرام فلم کوٹڈ گولیاں

دوا کو 25°C-20°C درجہ حرارت پر نمی اور روشنی سے محفوظ رکھیں۔
(درجہ حرارت کی حد 15°C سے 30°C ہے)

NEXT PHARMACEUTICAL
Manufactured by:
NEXT Pharmaceutical Products (Pvt.) Ltd.
Plot no. 44-A&B, Sunder Industrial Estate Lahore-Pakistan