For the use of a Registered Medical Practitioner or a Hospital or a Laboratory or a Specialist only

Cefixime & Ofloxacin Tablets

Cefzlan™ Tablets

Composition :
Each film coated tablet contains:
Cefixime IP as Trihydrate
eq. to Anhydrous Cefixime 200 mg Ofloxacin IP 200 mg Colours : Tartrazine & Titanium Dioxide IP

PHARMACEUTICAL FORM Film Coated Tablet.

THERAPEUTIC INDICATION
For the treatment of patients with typhoid fever and urinary tract infection in adults.

DOSAGE AND ADMINISTRATION
The recommended dosage for adults is 1 tablet once or twice daily or as directed by the Physician.
The duration and frequency of therapy depending upon the severity of infection. It is advised to adhere to the regimen as suggested by the Physician.
Method of administration: For oral use.

CONTRAINDICATIONS
Hypersensitivity to cephalosporins or quinolone antibiotics or to any of the excipients.
Ofloxacin is contraindicated if hypersensitivity to the active substance, to any other fluoroquinolone antibacterials. The use of ofloxacin is contraindicated in followings: In patients with a history of epilepsy or an existing central nervous system disorder with a lowered seizure threshold. In patients with a history of tendon disorders related to fluoroquinolone administration.
In children or growing adolescents, and in pregnant or breastfeeding women, since animal experiments do not entirely exclude the risk of damage to the growth-plate cartilage in the growing organism cannot be entirely excluded.
In patients with latent or actual defects in glucose-6-phosphate dehydrogenase activity because they may be prone to haemolytic reactions when treated with quinolone antibacterial agents.
The drug may cause low blood sugar and mental health related side effects. Low blood sugar levels, also called hypoglycaemia, can lead to coma. The mental health side effects more prominent and more cosistent across the systemic fluoroquinolone drug class. The mental health side effects to be added to or updated across all the fluoroquinolones are:
* disturbances in attention * disorientation * agitation * nervousness * memory impairment * serious disturbances in mental abilities called delirium.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE Cefixime
Severe cutaneous adverse reactions: Such as toxic epidermal necrolysis, Stevens-Johnson syndrome and drug rash with eosinophilia and systemic symptoms (DRESS) have been reported in some patients on cefixime. When severe cutaneous adverse reactions occur, cefixime should be discontinued and appropriate therapy and/or measures should be taken. Cefixime should be given with caution to patients who have shown hypersensitivity to other drugs.
Hypersensitivity to Penicillins: As with other cephalosporins, cefixime should be given with caution to patients with a history of hypersensitivity to penicillin, as there is some evidence of partial cross-allergenicity between the penicillins and cephalosporins.
Patients have had severe reactions (including anaphylaxis) to both classes of drugs. If an allergic effect occurs with Cefixime, the drug should be discontinued and the patient treated with appropriate agents if necessary.
Drug-induced haemolytic anaemia, including severe cases with a fatal outcome, has been described for cephalosporins (as a class). The recurrence of haemolytic anaemia after re-administration of cephalosporins in a patient with a history of cephalosporin (including cefixime)–associated haemolytic anaemia has also been reported.
As with other cephalosporins, cefixime may cause acute renal failure including tubulointerstitial nephritis as an underlying pathological condition. When acute renal failure occurs, cefixime should be discontinued and appropriate therapy and/or measures should be taken.
Renal impairment: Cefixime should be administered with caution in patients with markedly impaired renal function.
Paediatric use: Safety of cefixime in premature or newborn infant has not been established.
Treatment with broad spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by Clostridium difficile is a primary cause of antibiotic-associated diarrhoea. Pseudomembranous colitis is associated with the use of broad-spectrum antibiotics (including macrolides, semi-synthetic penicillins, lincosamides and cephalosporins); it is therefore important to consider its diagnosis in patients who develop diarrhoea in association with the use of antibiotics. Symptoms of pseudomembranous colitis may occur during or after antibiotic treatment.
Ofloxacin
Ofloxacin tablets are not the drug of first choice in pneumonia caused by Streptococcus pneumoniae or Chlamydia pneumoniae.
Methicillin-resistant S. aureus: Are very likely to possess co-resistance to fluoroquinolones, including ofloxacin. Therefore ofloxacin is not recommended for the treatment of known or suspected MRSA infections unless laboratory results have confirmed susceptibility of the organism to ofloxacin.
Resistance to fluoroquinolones of E. coli: The most common pathogen involved in urinary tract infections. Prescribers are advised to take into account the local prevalence of resistance in E. coli to fluoroquinolones.
Diseases caused by Clostridium Difficile: Diarrhoea, especially if severe, persistent and/or bloody, occurring during or after treatment with ofloxacin (including several weeks after treatment), may indicate a condition caused by Clostridium difficile, the most severe form of which is pseudomembranous colitis (CDAD).
Tendonitis, rarely observed with quinolones, may occasionally lead to rupture involving Achilles tendon in particular. Hypersensitivity and allergic reactions have been reported for fluoroquinolones after first administration.
Patients Predisposed to Seizures: Quinolones may lower the seizure threshold and may trigger seizures. Ofloxacin is contraindicated in patients with a history epilepsy or with a known predisposition to seizures.
Patients with impaired renal function: Since ofloxacin is eliminated primarily via the kidneys, the dose should be adjusted in patients with impaired renal function.
Patients with impaired liver function: Ofloxacin should be used with caution in patients with impaired liver function, as liver damage may occur.
Patients treated with vitamin K antagonists: Due to possible increase in coagulation tests (PT/INR) and/or bleeding in patients treated with fluoroquinolones, including ofloxacin, in combination with a vitamin K antagonist (e.g. warfarin), coagulation tests should be monitored when these drugs are given concomitantly.
Myasthenia gravis: Fluoroquinolones, including ofloxacin, have neuromuscular blocking activity and may exacerbate muscle weakness in patients with myasthenia gravis.
Superinfection: As with other antibiotics, the use of ofloxacin, especially if prolonged, may result in overgrowth of non-susceptible organisms, especially Enteracci, resistant strains of some organisms or Candida.
QT interval prolongation: Very rare cases of QT interval proplongation have been reported in patients taking fluoroquinolones.
Peripheral neuropathy: Sensory or sensorimotor peripheral neuropathy has been reported in patients receiving fluoroquinolones, including ofloxacin, which can be rapid in its onset.
Interference with laboratory tests: In patients treated with ofloxacin, determination of opiates or porphyrin levels in urine may give false-positive results. It may be necessary to confirm positive opiate or porphyrin screens by more specific methods.
Vision disorders: If vision becomes impaired or any effects on the eyes are experienced, an eye specialist should be consulted immediately.

DRUG INTERACTION Cefixime
Warfarin and Anticoagulants: In common with other cephalosporins, increases in prothrombin times have been noted in a few patients. Care should therefore be taken in patients receiving anticoagulation therapy. Cefixime should be administered with caution to patients receiving coumarin-type anticoagulants, e.g. warfarin potassium. Since cefixime may enhance effects of the anticoagulants, prolonged prothrombin time with or without bleeding may occur.
Carbamazepine: Elevated carbamazepine levels have been reported in postmarketing experience when cefixime is administered concomitantly. Drug monitoring may be of assistance in detecting alterations in carbamazepine plasma concentrations.
Ofloxacin
Antacids, Sucralfate, Metal Cations: Co-administered magnesium/aluminum antacids, sucralfate, zinc or iron preparations and didanosine chewable/buffered tablets can reduce absorption of ofloxacin tablets. Therefore, ofloxacin should be taken 2 hours before such preparations.
Theophylline, fenbufen or similar non-steroidal anti-inflammatory drugs: No pharmacokinetic interactions of ofloxacin were found with theophylline in a clinical study. However, a pronounced lowering of the cerebral seizure threshold may occur when quinolones are given concurrently with theophylline, nonsteroidal antiinflammatory drugs, or other agents, which lower the seizure threshold.
Probenecid, cimetidine, furosemide, and methotrexate: Probenecid decreased the total clearance of ofloxacin by 24%, and increased AUC by 16%. The proposed mechanism is a competition or inhibition for active transport at the renal tubular excretion. Caution should be exercised when ofloxacin is coadministered with drugs that affect the tubular renal secretion such as probenecid, cimetidine, furosemide and methotrexate.
Drugs known to prolong QT interval: Ofloxacin, like other fluoroquinolones, should be used with caution in patients receiving drugs known to prolong the QT interval (e.g. Class IA and III antiarrhythmics, tricyclic antidepressants, macrolides, and antipsychotics).
Vitamin K antagonists: Increased coagulation tests (PT/INR) and/or bleeding, which may be severe, have been reported in patients treated with ofloxacin in combination with a vitamin K antagonist (e.g. warfarin). Coagulation tests should, therefore, be monitored in patients treated with vitamin K antagonists because of a possible increase in the effect of coumarin derivatives.
Glibenclamide: Ofloxacin may cause a slight increase in plasma glibenclamide levels when administered concurrently, it is therefore recommended that patients treated concomitantly with ofloxacin and glibenclamide be monitored particularly closely. Since hypoglycaemia is then more likely to occur, close monitoring of blood sugar levels is recommended in such cases.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES Cefixime
In the case of side effects such as encephalopathy (which may include convulsion, confusion, impairment of consciousness, movement disorders), the patient should not operate machines or drive a vehicle.
Ofloxacin
Since there have been occasional reports of drowsiness/somnolence, impairment of skills, dizziness/vertigo and visual disturbances, which may impair the patient's ability to concentrate and react, and therefore may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery), patients should know how they react to ofloxacin before they drive or operate machinery.
These effects may be enhanced by alcohol.

ADVERSE DRUG REACTIONS / UNDESIRABLE EFFECTS Cefixime
Acute generalized exanthematous pustulosis (AGEP): Beta-lactams, including cefixime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment.
Mouth ulceration: It is reported that Cefixime formulations may cause mouth ulceration.
The majority of adverse reactions observed in clinical trials were mild and self-limiting in nature. The following are the undesirable effects
Reported with Cefixime: Diarrhea, loose stools, abdominal pain, dyspepsia, nausea, and vomiting. Several cases of documented pseudomembranous colitis were identified during the studies. The onset of pseudomembranous colitis symptoms may occur during or after therapy. Anaphylactic/anaphylactoid reactions (including shock and fatalities), skin rashes, urticaria, drug fever, pruritus, angioedema, and facial edema. Erythema multiforme, Stevens-Johnson syndrome, and serum sickness-like reactions have been reported. Transient elevations in SGPT, SGOT, alkaline phosphatase, hepatitis, jaundice. Transient elevations in BUN or creatinine, acute renal failure.Headaches, dizziness, seizures. Transient thrombocytopenia, leukopenia, neutropenia, and eosinophilia. Prolongation in prothrombin time was seen rarely.Hyperbilirubinemia.Genital pruritus, vaginitis, candidiasis, toxic epidermal necrolysis.
Diarrhoea has been more commonly associated with higher doses. Some cases of moderate to severe diarrhoea have been reported; this has occasionally warranted cessation of therapy. cefixime should be discontinued if marked diarrhoea occurs.
Ofloxacin
Stevens-Johnson syndrome or Toxic epidermal necrolysis: Cases of severe bullous skin reactions such as Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) have been reported with ofloxacin. Patients should be advised to contact their doctor immediately prior to continuing treatment if skin and/or mucosal reactions occur.
Hypoglycemia: As with all quinolones, disturbances in blood glucose, including both hypoglycaemia and hyperglycaemia have been reported, usually in diabetic patients receiving concomitant treatment with an oral hypoglycaemic agent (e.g., glibenclamide) or with insulin.
Psychotic reactions, have been reported in patients receiving fluoroquinolones including ofloxacin.
The information given below is based on data from clinical studies and on extensive post marketing experience.
General: Uncommon: Fungal infection, Pathogen resistance, Agitation, Sleep disorder, Insomnia, Dizziness, Headache, Eye irritation, Vertigo, Cough, Nasopharyngitis, Abdominal pain, Diarrhoea, Nausea, Vomiting, Pruritus, Rash. Rare: Anaphylactic reaction, Anaphylactoid reaction, Angioedema, Anorexia, Psychotic disorder (for e.g. hallucination), Anxiety, Confusional state, Nightmares, Depression, Somnolence, Paraesthesia, Dysgeusia, Parosmia, Visual disturbance, Tachycardia, Hypotension, Dyspnoea, Bronchospasm, Enterocolitis, sometimes haemorrhagic, Hepatic enzymes increased, Blood bilirubin increased, Urticaria, Hot flushes, Hyperhidrosis, Pustular rash, Tendonitis, Serum creatinine increased. Very Rare: Anaemia, Haemolytic anaemia, Leucopenia, Eosinophilia, Thrombocytopenia, Anaphylactic shock, Anaphylactoid shock, Peripheral sensory neuropathy, Peripheral sensory motor neuropathy, Convulsion, Extra-pyramidal symptoms or other disorders of muscular coordination, Tinnitus, Hearing loss, Jaundice cholestatic, Erythema multiforme, Photo-sensitivity reaction, Drug eruption, Vascular purpura, Vasculitis, Arthralgia, Myalgia, Tendon rupture, Acute renal failure.

OVERDOSE
There is a risk of encephalopathy in cases of administration of beta-lactam antibiotics, including cefixime, particularly in case of overdose or renal impairment.
The most important signs with Ofloxacin to be expected following acute overdose are CNS symptoms such as confusion, dizziness, impairment of consciousness and convulsive seizures increases in QT interval as well as gastrointestinal reactions such as nausea and mucosalerosions.

PHARMACOLOGICAL PROPERTIES
Cefixime is an oral third generationcephalosporin which has marked in vitro bactericidal activity against a wide variety of Gram-positive and Gram-negative organisms.Clinical efficacy has been demonstrated in infections caused by commonly occurring pathogens including Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Proteus mirabilis, Klebsiella species, Haemophilus influenzae (beta-lactamase positive and negative), Branhamella catarrhalis (beta-lactamase positive and negative) and Enterobacter species. It is highly stable in the presence of beta-lactamase enzymes. Like all beta-lactam antibiotics, cefixime binds to specific penicillin-binding proteins (PBPs) located inside the bacterial cell wall, causing the inhibition of the third and last stage of bacterial cell wall synthesis. Cell lysis is then mediated by bacterial cell wall autolytic enzymes such as autolysins; it is possible that cefixime interferes with an autolysin inhibitor.
Ofloxacin is a quinolone/fluoroquinolone antibiotic. Ofloxacin is bactericidal and its mode of action depends on blocking of bacterial DNA replication by binding itself to an enzyme called DNA gyrase, which allows the untwisting required to replicate one DNA double helix into two. Notably the drug has 100 times higher affinity for bacterial DNA gyrase than for mammalian. Ofloxacin is a broad-spectrum antibiotic that is active against both Gram-positive and Gram-negative bacteria. Ofloxacin acts on DNA gyrase and toposiomerase IV, enzymes which, like human topoisomerase, prevents the excessive supercoiling of DNA during replication or transcription. By inhibiting their function, the drug thereby inhibits normal cell division.

PHARMACOKINETIC PROPERTIES Absorption
Only 40 to 50 % of an oral dose of Cefixime is absorbed from gastrointestinal tract, whether taken before or after meals, although the rate of absorption may be decreased in the presence of food. Ofloxacin is rapidly and well absorbed from the gastrointestinal tract. Oral bioavailability is almost 100%. Absorption may be delayed by the presence of food, but the extent of absorption is not substantially affected.
Distribution
About 65 % of cefixime in the circulation is bound to plasma proteins.
The plasma protein binding of ofloxacin was approximately 25%.
Metabolism
Metabolites of cefixime have not been isolated from human serum or urine.
The biotransformation of ofloxacin was below 5%. The two main metabolites found in the urine were N-desmethyl-ofloxacin and ofloxacin-Noxide.
Excretion
Cefixime is predominantly eliminated as unchanged drug in the urine. Glomerular filtration is considered the predominant mechanism.
Excretion of ofloxacin is primarily renal. Between 80 and 90% of the dose were recovered from the urine as unchanged substance. Ofloxacin was present in the bile in glucuronidised form. The plasma half-life is prolonged in persons with renal insufficiency; total and renal clearance decrease in accordance with the creatinine clearance. In renal insufficiency the dose should be reduced.

INCOMPATIBILITES None stated.

PACKING INFORMATION 10X10 Tablets

STORAGE INSTRUCTIONS
Store protected from light & moisture, at a temperature not exceeding 30°C.

Keep out of reach of children.

Manufactured by : Malik Lifesciences Pvt. Ltd.
(A subsidiary of Akums Drugs & Pharmaceuticals Ltd.) Plot No.16, Vardhman Indl. Estate, Vill- Bahadarpur Saini, N.H.58, Haridwar-247667 (Uttarakhand)

Manufactured in India for :
Cafoli™ LIFECARE
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(An ISO 9001 : 2015 Certified Co.)
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