For the use of a Registered Medical Practitioner only

℞ Ofloxacin & Cefixime Tablets

Ofcef*

WARNING: SERIOUS ADVERSE REACTIONS INCLUDING TENDINITIS, TENDON RUPTURE, PERIPHERAL NEUROPATHY, CENTRAL NERVOUS SYSTEM EFFECTS AND EXACERBATION OF MYASTHENIA GRAVIS

Fluoroquinolones, including ofloxacin, have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together, including:

- Tendinitis and tendon rupture
- Peripheral neuropathy
- Central nervous system effects

Discontinue ofloxacin immediately and avoid the use of fluoroquinolones, including ofloxacin, in patients who experience any of these serious adverse reactions

- Fluoroquinolones, including ofloxacin, may exacerbate muscle weakness in persons with myasthenia gravis. Avoid ofloxacin in patients with a known history of myasthenia gravis.
- Because fluoroquinolones, including ofloxacin, have been associated with serious adverse reactions, reserve ofloxacin for us e in patients who have no alternative treatment options for the following indications:
- Acute exacerbation of chronic bronchitis
- Uncomplicated cystitis

Fluoroquinolone may cause Low blood sugar and Mental health related side effects

Composition :

Each film coated tablet contains:
Ofloxacin IP.....200 mg
Cefixime IP as Trihydrate
eq. to Anhydrous Cefixime.....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.

DOSAGEAND 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 ofioxacin is contraindicated in followings: In patents 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 patents 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.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Cefixime

Severe cutaneous adverse reactions: Such as toxic epidermal necrolysis, Stevens-Johnson syndrome and drug rash with eosinophilla 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 penicillin 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 newbom 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 penicillin, 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

Methicillin-resistant S. aureus are very likely to possess co-resistance to fluoroquinolones, including ofioxacin. 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 (and commonly recommended antibacterial agents for the treatment of MRSA-infections are considered inappropriate).

Ofloxacin is not the drug of first choice for pneumonia caused by Pneumococci or Mycoplama or infection caused by f3-haemolytic Streptococci.

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. cell to fluoroquinolones.

Hypersensitivity and allergic reactions

Hypersensitivity and allergic reactions have been reported for fluoroquinolones after first administration. Anaphylactic and anaphylactoid reactions can progress to life-threatening shock, even after the first administration. In these cases ofioxacin should be discontinued and suitable treatment (e.g treatment for shock) should be initiated.

Severe bullous reactions

Cases of severe bullous skin reactions such as Stevens-Johnson syndrome or toxic epidermal necrolysis 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.

Clostridium difficile-associated disease

Diarrhoea, particularly if severe, persistent and/or bloody, during or after treatment with ofloxacin (including several weeks after treatment), may be symptomatic of pseudo-membranous colitis (CDAD). CDAD may range in severity from mild to life threatening, the most severe form which is pseudomembranous colitis. It is therefore important to consider this diagnosis in patients who develop serious diarrhoea during or after treatment with ofioxacin If pseudo-membranous colitis is suspected, ofloxacin must be stopped immediately.

Appropriate specific antibiotic therapy must be started without delay (e.g. oral vancomycin, oral teicoplanin or metronidazole). Products inhibiting the peristalsis are contraindicated in this clinical situation.

Patients predisposed to seizures

Quinolones may lower the seizure threshold and may trigger seizures. Ofioxacin is contraindicated in patients with a history of epilepsy and, as with other quinolones, ofloxacin should be used with extreme caution in patents predisposed to seizures.

Such patients may be patients with pre-existing central nervous system lesions, concomitant treatment with fenbufen and similar non-steroidal anti-inflammatory drugs or with drugs which lower the cerebral seizure threshold, such as theophyl line.

In case of convulsive seizures, treatment with ofloxacin should be discontinued.

Tendonitis

Tendonitis, rarely observed with quinolones, may occasionally lead to rupture involving Achilles tendon in particular. Tendinitis and tendon rupture, sometimes bilateral, may occur within 48 hours of starting treatment with ofloxacin and have been reported up to several months after discontinuation of. The risk of tendinitis and tendon rupture is increased in patients aged over 60 years and in patents using corticosteroids. The daily dose should be adjusted in elderly patients based on creatinine clearance. Close monitoring of these patients is therefore necessary if they are prescribed ofloxacin. All patients should consult their physician if they experience symptoms of tendinitis. If tendinitis is suspected, treatment with ofloxacin must be halted immediately, and appropriate treatment (e.g. immobilisation) must be initiated for the affected tendon.

Patients with renal impairment

Since ofioxacin is mainly excreted by the kidneys, the dose of ofloxacin should be adjusted in patients with renal impairment.

QT interval prolongation

Very rare cases of QT interval prolongation have been reported in patients taking fluoroquinolones. Caution should be taken when using fluoroquinolones, including ofloxacin, in patients with known risk factors for prolongation of the QT interval such as, for example:

- Congenital long QT syndrome
- Concomitant use of drugs that are known to prolong the QT interval (e.g. Class lA and III anti-arrhythmics, tricyclic antidepressants, macrolides, antipsychotics)
- Uncorrected electrolyte imbalance (e.g. hypokalaemia, hypomagnesaemia)
- Cardiac disease (e.g. heart failure, myocardial infarction, bradycardia)
- Elderly patients and women may be more sensitive to QTc-prolonging medications. Therefore, caution should be taken when using fluoroquinolones, including Ofloxacin, in these populations.

Patients with history of psychotic disorder

Psychotic reactions have been reported in patients receiving fluoroquinolones. In some cases these have progressed to suicidal thoughts or self-endangering behaviour including suicide attempt, sometimes after a single dose. In the event that a patient develops these reactions, ofioxacin should be discontinued and appropriate measures instituted.

Ofloxacin should be used with caution in patients with a history of psychotic disorder or in patients with psychiatric disease.

Patients with impaired liver function

Ofloxacin should be used with caution in patients with impaired liver function, as liver damage may occur. Cases of fulminant hepatitis potentially leading to liver failure (including fatal cases) have been reported with fluoroquinolones. Patents should be advised to stop treatment and contact their doctor if signs and symptoms of hepatic disease develop such as anorexia, jaundice, dark urine, omits or tender abdomen.

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. Post-marketing serious adverse reactions, including deaths and the requirement for respiratory support, have been associated with fluoroquinolone use in patents with myasthenia gravis. Ofioxacin is not recommended in patients with a known history of myasthenia gravis.

Prevention of photosensitisation

Photosensitisation has been reported with ofloxacin. It is recommended that patients should not expose themselves unnecessarily to strong sunlight or to artificial UV rays (e.g. sunray lamp, solarium), during treatment and for 48 hours following treatment discontinuation in order to prevent photosensitisation.

Superinfection

As with other antibiotics, the use of ofloxacin, especially if prolonged, may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If secondary infection occurs during therapy, appropriate measures should be taken.

Peripheral neuropathy

Sensory or sensorimotor peripheral neuropathy has been reported in patients receiving fluoroquinolones, including ofloxacin, which can be rapid in its onset. Ofloxacin should be discontinued if the patient experiences symptoms of neuropathy in order to prevent the development of an irreversible condition.

Dysglycaemia

As with all quinolones, disturbances in blood glucose, including both hyperglycaemia and hypoglycaemia have been reported, usually in diabetic patients receiving concomitant treatment with an oral hypoglycaemic agent (e.g. glibenclamide) or with insulin. Cases of hypoglycaemic coma have been reported. In these diabetic patients, careful monitoring of blood glucose is recommended.

Patients with glucose-6-phosphate-dehydrogenase deficiency

Patients with latent or diagnosed glucose-6-phosphate-dehydrogenase deficiency may be predisposed to haemolytic reactions if they are treated with quinolones. Therefore, if ofloxacin has to be used in these patients, potential occurrence of haemolysis should be monitored.

Vision disorders

If vision becomes impaired or any effects on the eyes are experienced, an eye specialist should be consulted immediately.

Interference with laboratorytests

In patients treated with ofloxacin, determination of opiates in urine may give false-positive results. It may be necessary to confirm positive opiate screens by more specific method.

Patients with rare hereditary disorders.

Patients with rare hereditary disorders of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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 lowerthe 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 lAand 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

Ceflxlme

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 ordrive 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.

UNDESIRABLE EFFECTS

Ceflxlme

Acute Generalized exanthematous oustulosis (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.

Cefixime is generally well tolerated. The majority of adverse reactions observed in clinical trials were mild and self-limiting in nature. The following adverse reaction (Preferred term or equivalent) will be considered listed:

Blood and lymphatic system disorders: eosinophilia, hypereosinophilia, agranulocytosis, leucopaenia, neutropaenia, granulocytopaenia, haemolytic anaemia, thrombocytopaenia, and thrombocytosis.

Gastrointestinal disorders: abdominal pain, diarrhoea*, dyspepsia, nausea, vomiting, and flatulence.

Hepatobiliarydisorders: Jaundice.

Infections and infestations: pseudomembranous colitis.

Investigations: aspartate aminotransferase increased, alanine aminotransferase increased, blood bilirubin increased, blood urea increased, blood creatinine increased.

Nervous system disorders: Dizziness, Headache, Cases of convulsions have been reported with cephalosporins, including cefixime (frequency not known), 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 (frequency not known)**.

Respiratory thoracic and mediastinal disorders: Dyspnoea.

Renal and urinary disorders: Renal failure acute, including tubulointerstitial nephritis as an underlying pathological condition.

Immune system disorders, administrative site conditions, skin and subcutaneous tissue disorders: anaphylactic reaction, serum sickness-like reaction, DRESS, pruritus, rash, drug fever, arthralgia, erythema multiforme, sevens Johnson syndrome, toxic epidermal necrolysis, angioedema, urticaria, pyrexia, face oedema, genital pruritus, and vaginitis.

The above mentioned listed adverse reactions have been observed during clinical studies and/or during marketed use.

*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.

** Cannot be estimated from available data.

Ofloxacin

Low blood sugar and mental health related side effects: The drug may cause low blood sugar and mental health related side effects. Low blood sugar levels, also called as hypoglycemia, can lead to coma. The mental health side effects are more prominent and more consistent across the systemic fluoroquinolone drug class. The mental side effects to fluoroquinolones are:

- Disturbance in attention,
- Disorientation,
- Agitation,
- Nervousness,
- Memory impairment,
- Serious disturbances in mental abilities called delirium.

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.

The information given below is based on data from clinical studies and on extensive post marketing experience.

Infections and infestations: Uncommon: Fungal infection, Pathogen resistance.

Blood and lymphatic system disorders: Very rare: Anaemia, haemolytic anaemia, leucopenia, eosinophilia, and thrombocytopenia. Not known: Agranulocytosis, bone marrow failure, pancytopenia.

Immune system disorders: Rare: Anaphylactic reaction*, anaphylactoid reaction*, angioedema*. Very rare: Anaphylactic shock*, anaphylactoid shock*.

Metabolism and Nutrition disorders: Rare:Anorexia. Not known: Hypoglycaemia in diabetics treated with hypoglycaemic agents, Hyperglycaemia, Hypoglycaemic coma.

*Psychiatric disorders**:* Uncommon: Agitation, sleep disorder, insomnia. Rare: Psychotic disorder (for e.g. hallucination), anxiety, confusional state, nightmares, depression. Not known: Psychotic disorder and depression with self-endangering behaviour including suicidal ideation or suicide attempt, nervousness.

*Nervous system disorders**:* Uncommon: Dizziness, headache. Rare: Somnolence, paraesthesia, dysgeusia, parosmia. Very rare: Peripheral sensory neuropathy*, peripheral sensory motor neuropathy*, convulsion*, extra-pyramidal symptoms or other disorders of muscular coordination. Not known: Tremor, dykinesia, ageusia, syncope, benign intracranial hypertension (pseudotumorcerebri).

*Eye disorders**:* Uncommon: Eye irritation. Very rare: Visual disturbance. Not known: Uveitis.

Ear and labyrinth disorders**: Uncommon: Vertigo. Very rare: Tinnitus, hearing loss. Not known: Hearing impaired.

Cardiac disorders: Rare: Tachycardia. Not known: Ventricular arrhythmias and torsades de pointes (reported predominantly in patients with risk factors for QT prolongation), ECG QT prolonged.

Vasculardisorders: Rare: Hypotension.

Respiratory, thoracic and mediastinal disorders: Uncommon: Cough, Nasopharyngitis. Rare: Dyspnoea, bronchospasm. Not known: Allergic pneumonitis, severe dyspnoea.

Gastrointestinal disorders: Uncommon:Abdominal pain, diarrhoea, nausea, vomiting. Rare: Enterocolitis, sometimes haemorrhagic. Very rare: Pseudomembranous colitis*. Not known: Dyspepsia, flatulence, constipation, pancreatitis.

Hepatobiliary disorders: Rare: Hepatic enzymes increased (ALAT, ASAT, LDH, gamma-GT and/or alkaline phosphatase), blood bilirubin increased. Very rare: Jaundice cholestatic. Not known: Hepatitis, which may be severe, *severe liver injury, including cases of acute liver failure; sometimes fatal, have been reported with ofloxacin, primarily in patients with underlying liver disorders.

Skin and subcutaneous tissue disorders: Uncommon: Pruritus, rash. Rare: Urticaria, hot flushes, hyperhidrosis, pustular rash. Very rare: Erythema multiforme, toxic epidermal necrolysis, photo-sensitivity reaction*, drug eruption, vascular purpura, vasculitis, which can lead in exceptional cases to skin necrosis. Not known: Stevens-Johnson syndrome, acute generalised exanthemous pustulosis, drug rash, stomatitis, exfoliative dermatitis.

*Musculoskeletal and connective tissue disorders**:* Rare: Tendonitis. Very rare: Arthralgia, myalgia, tendon rupture (e.g. Achilles tendon)which may occur within 48 hours of treatment start and may be bilateral. Not known: Rhabdomyolysis and/or myopathy, muscular weakness, muscle tear, muscle rupture, ligament rupture, arthritis.

Renal and urinary disorders: Rare: Serum creatinine increased. Very rare:Acute renal failure. Not known:Acute interstitial nephritis.

Congenital, familial and genetic disorders: Not known: Attacks of porphyria in patients with porphyria.

General disorders and administration site conditions':* Not known:Asthenia, pyrexia, pain (including pain in back, chest and extremities).

* postmarketing experience

** Very rare cases of prolonged (up to months or years), disabling and potentially irreversible serious drug reactions affecting several, sometimes multiple, system organ classes and senses (including reactions such as tendinitis, tendon rupture, arthralgia, pain in extremities, gait disturbance, neuropathies associated with paraesthesia, depression, fatigue, memory impairment, sleep disorders, and impairment of hearing, vision, taste and smell) have been reported in association with the use of quinolones and fluoroquinolones in some cases irrespective of pm-existing risk factors.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Kindly report any suspected adverse reactions to pharmavigil@jbpharma.com

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

Pharmacodynamic Properties

Cefixime

Cefixime is an oral third generation cephalosporin 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

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 replicating 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-N-oxide.

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.

STORAGE INSTRUCTIONS

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

Keep out of reach of children.

PACKAGING INFORMATION

Blister of 10 tablets

Marketed by :
J. B. CHEMICALS & PHARMACEUTICALS LTD.
Neelam Centre, 'B' Wing, Hind Cycle Road,
Worli, Mumbai - 400 030. India.
* Trade Mark under registration

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Note: This prescribing information is applicable for India Market only