Ofloscot
Tablets

اوفلوسکاٹ ٹیبلٹس

COMPOSITION:
Each Film coated contains:
Ofloxacin……..…200 & 400 mg

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 reaction that have occurred together, including:

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

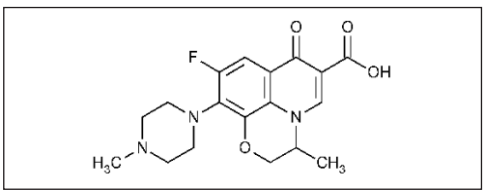
Discontinue Ofloxacin immediately and avoid the use of Fluoroquinolones, including Ofloxacin in patients who experience any of these serious adverse reactions.

Fluoroquinolones, including Ofloxacin may exacerbate muscle weakness in patients with myasthenia gravis. Avoid Ofloxacin in patients with known history of myasthenia gravis.

As Fluoroquinolones, including Ofloxacin have been associated with serious adverse reactions, reserve Ofloxacin for use in patients who have no alternative treatment options for the following indications:

- Acute exacerbation of chronic bronchitis
- Acute sinusitis
- Acute uncomplicated cystitis

DESCRIPTION
OFLOSCOT Tablets is a synthetic broad-spectrum antimicrobial agent for oral administration. Chemically, ofloxacin, a fluorinated carboxyquinolone, is the racemate, (±)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7 oxo-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid. The chemical structure is:



CLINICAL PHARMACOLOGY:
Mechanism of Action
Ofloxacin is a quinolone antimicrobial agent. The mechanism of action of ofloxacin and other fluoroquinolone antimicrobials involves inhibition of bacterial topoisomerase IV and DNA gyrase (both of which are type II topoisomerases), enzymes required for DNA replication, transcription, repair and recombination. Ofloxacin has in vitro activity against a wide range of gram-negative and gram-positive microorganisms. Ofloxacin is often bactericidal at concentrations equal to or slightly greater than inhibitory concentrations. Fluoroquinolones, including ofloxacin, differ in chemical structure and mode of action from aminoglycosides, macrolides and β-lactam antibiotics, including penicillins. Fluoroquinolones may, therefore, be active against bacteria resistant to these antimicrobials.
Pharmacokinetics:
Following oral administration, the bioavailability of ofloxacin in the tablet formulation is approximately 98%. Maximum serum concentrations are achieved one to two hours after an oral dose. Absorption of ofloxacin after single or multiple doses of 200 to 400 mg is predictable, and the amount of drug absorbed increases proportionately with the dose. Ofloxacin has biphasic elimination. Following multiple oral doses at steady-state administration, the half-lives are approximately 4-5 hours and 20-25 hours. However, the longer half-life represents less than 5% of the total AUC. Accumulation at steady-state can be estimated using a half-life of 9 hours. The total clearance and volume of distribution are approximately similar after single or multiple doses. Elimination is mainly by renal excretion.

MICROBIOLOGY
Ofloxacin has been shown to be active against most strains of the following microorganisms both in vitro and in clinical infections:
Aerobic Gram-positive Microorganisms: Staphylococcus aureus (methicillin-susceptible strains) Streptococcus pneumoniae (penicillin-susceptible strains) Streptococcus pyogenes.
Aerobic Gram-negative Microorganisms: Citrobacter (diversus) koseri Enterobacter aerogenes Escherichia coli Haemophilus influenzae Klebsiella pneumoniae Neisseria gonorrhoeae Proteus mirabilis Pseudomonas aeruginosa As with other drugs in this class, some strains of Pseudomonas aeruginosa may develop resistance fairly rapidly during treatment with ofloxacin.
Aerobic Gram-positive Microorganisms: Staphylococcus epidermidis (methicillin-susceptible strains) Staphylococcus saprophyticus Streptococcus pneumoniae (penicillin-resistant strains).
Aerobic Gram-negative Microorganisms: Acinetobacter calcoaceticus Bordetella pertussis Citrobacter freundii Enterobacter cloacae Haemophilus ducreyi Klebsiella oxytoca Moraxella catarrhalis Morganella morganii Proteus vulgaris Providencia rettgeri Providencia stuartii Serratia marcescens.
Anaerobic Microorganisms: Clostridium perfringes
Other Microorganisms: Chlamydia pneumoniae Gardnerella vaginalis Legionella pneumophila Mycoplasma hominis Mycoplasma pneumoniae Ureaplasma urealyticum.

Ofloxacin is not active against Treponema pallidum.

INDICATIONS AND USAGE

- To reduce the development of drug-resistant bacteria and maintain the effectiveness of OFLOSCOT Tablets and other antibacterial drugs, OFLOSCOT Tablets should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy
- ***Acute bacterial exacerbations of chronic bronchitis:*** Ofloxacin is indicated in acute bacterial exacerbations of chronic bronchitis due to Haemophilus influenzae or Streptococcus pneumoniae.
- ***Community-acquired Pneumonia:*** Ofloxacin is indicated in community-acquired Pneumonia due to Haemophilus influenzae or Streptococcus pneumoniae.
- ***Uncomplicated skin and skin structure infections:*** Ofloxacin is indicated in uncomplicated skin and skin structure due to methicillin-susceptible Staphylococcus aureus, Streptococcus pyogenes, or Proteus mirabilis.
- ***Acute, uncomplicated urethral and cervical gonorrhea:*** Ofloxacin is indicated in acute, uncomplicated urethral and cervical gonorrhea due to Neisseria gonorrhoeae.
- ***Nongonococcal urethritis and cervicitis:*** Ofloxacin is indicated in nongonococcal urethritis and cervicitis due to Chlamydia trachomatis
- ***Mixed Infections of the urethra and cervix:*** Ofloxacin is indicated in mixed Infections of the urethra and cervix due to Chlamydia trachomatis and Neisseria gonorrhoeae
- ***Acute pelvic inflammatory disease (including severe infection):*** Ofloxacin is indicated in Acute pelvic inflammatory disease (including severe infection) due to Chlamydia trachomatis and/or Neisseria gonorrhoeae.
- ***Uncomplicated cystitis:*** Ofloxacin is indicated in Uncomplicated cystitis due to Citrobacter diversus, Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, or Pseudomonas aeruginosa.
- ***Complicated urinary tract infections:*** Ofloxacin is indicated in Complicated urinary tract infections due to Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Citrobacter diversus, or Pseudomonas aeruginosa.
- ***Prostatitis:*** Ofloxacin is indicated in Prostatitis due to Escherichia coli.

CONTRAINDICATIONS
OFLOSCOT (ofloxacin tablets) Tablets is contraindicated in persons with a history of hypersensitivity associated with the use of ofloxacin or any member of the quinolone group of antimicrobial agents.

DRUG INTERACTIONS
Antacids, Sucralfate, Metal Cations, Multivitamins:
Quinolones form chelates with alkaline earth and transition metal cations. Administration of quinolones with antacids containing calcium, magnesium, or aluminum, with sucralfate, with divalent or trivalent cations such as iron, or with multivitamins containing zinc may substantially interfere with the absorption of quinolones resulting in systemic levels considerably lower than desired. These agents should not be taken within the two-hour period before or within the two-hour period after ofloxacin administration.
Caffeine:
Interactions between ofloxacin and caffeine have not been detected
Cimetidine:
Cimetidine has demonstrated interference with the elimination of some quinolones. This interference has resulted in significant increases in half-life and AUC of some quinolones. The potential for interaction between ofloxacin and cimetidine has not been studied.
Cyclosporine:
Elevated serum levels of cyclosporine have been reported with concomitant use of cyclosporine with some other quinolones. The potential for interaction between ofloxacin and cyclosporine has not been studied.
Probenecid:
The concomitant use of probenecid with certain other quinolones has been reported to affect renal tubular secretion. The effect of probenecid on the elimination of ofloxacin has not been studied.
Theophylline:
Steady-state theophylline levels may increase when ofloxacin and theophylline are administered concurrently. As with other quinolones, concomitant administration of ofloxacin may prolong the half-life of theophylline, elevate serum theophylline levels, and increase the risk of theophylline-related adverse reactions. Theophylline levels should be closely monitored and theophylline dosage adjustments made, if appropriate, when ofloxacin is co-administered. Adverse reactions (including seizures) may occur with or without an elevation in the serum theophylline level.
Warfarin:
Some quinolones have been reported to enhance the effects of the oral anticoagulant warfarin or its derivatives. Therefore, if a quinolone antimicrobial is administered concomitantly with warfarin or its derivatives, the prothrombin time or other suitable coagulation test should be closely monitored
Antidiabetic agents:
Since disturbances of blood glucose, including hyperglycemia and hypoglycemia, have been reported in patients treated concurrently with quinolones and an antidiabetic agent, careful monitoring of blood glucose is recommended when these agents are used concomitantly.
Interaction with Laboratory or Diagnostic Testing:
Some quinolones, including ofloxacin, may produce false-positive urine screening results for opiates using commercially available immunoassay kits. Confirmation of positive opiate screens by more specific methods may be necessary.

ADVERSE REACTIONS

Table 1: Medically important adverse reactions that occured in less than 1% regardless of relationship to drug.

System Organ Class	Adverse Reactions
Body as a Whole	Asthenia, chills, malaise, extremity pain, pain, epistaxis
Cardiovascular	Cardiac arrest, edema, hypertension, hypotension, palpitations vasodilation
Nervous System	Seizures, anxiety, cognitive change, depression, dream abnormality, euphoria, hallucinations, paresthesia, syncope, vertigo, tremor, confusion
Gastrointestinal	Dyspepsia
Musculoskeletal System	Arthralgia, myalgia
Skin/Hypersensitivity	Angioedema, diaphoresis, urticaria, vasculitis
Urinary System	Dysuria, urinary frequency, urinary retention
Nutritional/Metabolic	Thirst, weight loss
Respiratory	Respiratory arrest, cough, rhinorrhea
Genital/Reproductive System	Burning, irritation, pain and rash of the female genitalia, dysmenorrhea, menorrhagia, metrorrhagia

WARNINGS AND PRECAUTIONS

Tendinopathy and Tendon Rupture: Fluoroquinolones, including(OFLOSCOT), are associated with an increased risk of tendinitis and tendon rupture in all ages. This adverse reaction most frequently involves the Achilles tendon, and rupture of the Achilles tendon may require surgical repair. Tendinitis and tendon rupture in the rotator cuff (the shoulder), the hand, the biceps, the thumb and other tendon sites have also been reported. The risk of developing fluoroquinolone-associated tendinitis and tendon rupture is further increased in older patients usually over 60 years of age, in those taking corticosteroid drugs, and in patients with kidney, heart or lung transplants. Factors, in addition to age and corticosteroid use, that may independently increase the risk of tendon rupture include strenuous physical activity, renal failure, and previous tendon disorders such as rheumatoid arthritis. Tendinitis and tendon rupture have also occurred in patients taking fluoroquinolones who do not have the above risk factors. Tendon rupture can occur during or after completion of therapy; cases occurring up to several months after completion of therapy have been reported. OFLOSCOT should be discontinued if the patient experiences pain, swelling, inflammation or rupture of a tendon. Patients should be advised to rest at the first sign of tendinitis or tendon rupture, and to contact their healthcare provider regarding changing to a non-quinolone antimicrobial drug.

Hypersensitivity Reactions: Serious and occasionally fatal hypersensitivity and/or anaphylactic reactions have been reported in patients receiving therapy with quinolones, including ofloxacin. These reactions often occur following the first dose. Some reactions have been accompanied by cardiovascular collapse, hypotension/shock, seizure, loss of consciousness, tingling, angioedema (including tongue, laryngeal, throat, or facial edema/swelling), airway obstruction (including bronchospasm, shortness of breath, and acute respiratory distress), dyspnea, urticaria, itching, and other serious skin reactions. This drug should be discontinued immediately at the first appearance of a skin rash or any other sign of hypersensitivity. Serious acute hypersensitivity reactions may require treatment with epinephrine and other resuscitative measures, including oxygen, intravenous fluids, antihistamines, corticosteroids, pressor amines, and airway management, as clinically indicated.

Peripheral neuropathy: Ofloxacin should be discontinued if the patient experiences symptoms of neuropathy including pain, burning, tingling, numbness, and/or weakness or other alterations of sensation including light touch, pain, temperature, position sense, and vibratory sensation in order to prevent the development of an irreversible condition.

Clostridium difficile associated diarrhea (CDAD): CDAD has been reported with use of nearly all antibacterial agents, including (OFLOSCOT), 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.

Renal or hepatic insufficiency/impairment: Administer ofloxacin with caution in the presence of renal or hepatic insufficiency/impairment. In patients with known or suspected renal or hepatic insufficiency/impairment, careful clinical observation and appropriate laboratory studies should be performed prior to and during therapy since elimination of ofloxacin may be reduced.

Photosensitivity/phototoxicity reactions: Moderate to severe photosensitivity/phototoxicity reactions, the latter of which may manifest as exaggerated sunburn reactions (e.g., burning, erythema, exudation, vesicles, blistering, edema) involving areas exposed to light (typically the face, "V" area of the neck, extensor surfaces of the forearms, dorsa of the hands), can be associated with the use of quinolones after sun or UV light exposure. Therefore, excessive exposure to these sources of light should be avoided. Drug therapy should be discontinued if photosensitivity/phototoxicity occurs.

SPECAIL POPULATIONS

Pregnancy: Teratogenic Effects. Pregnancy Category C. Ofloxacin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: In lactating females, a single oral 200-mg dose of ofloxacin resulted in concentrations of ofloxacin in milk that were similar to those found in plasma. Because of the potential for serious adverse reactions from ofloxacin in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in pediatric patients and adolescents below the age of 18 years have not been established.

Geriatric Use : Geriatric patients are at increased risk for developing severe tendon disorders including tendon rupture when being treated with a fluoroquinolone.

Elderly patients: may be more sensitive to drug-associated effects on the QT interval. Therefore, precaution should be taken when using ofloxacin with concomitant drugs that can result in prolongation of the QT interval (e.g. Class IA or Class III antiarrhythmics) or in patients with risk factors for Torsade de pointes (e.g. known QT prolongation, uncorrected hypokalemia).

DOSAGE AND ADMINISTRATION

The usual dose of OFLOSCOT Tablets is 200 mg to 400 mg orally every 12 h as described in the following dosing chart. These recommendations apply to patients with normal renal function.

Table 2: Dosage Guidelines

Infection	Unit Dose	Frequency	Duration	Daily Dose
Acute Bacterial Exacerbation of Chronic Bronchitis	400 mg	q12h	10 days	800 mg
Comm. Acquired Pneumonia	400 mg	q12h	10 days	800 mg
Uncomplicated Skin and Skin Structure Infections	400 mg	q12h	10 days	800 mg
Acute, Uncomplicated Urethral and Cervical Gonorrhea	400 mg	single dose	01 day	400 mg
Nongonococcal Cervicitis/Urethritis due to C. trachomatis	300 mg	q12h	07 days	600 mg
Mixed Infection of the urethra and cervix due to C. trachomatis and N. gonorrhoeae	300 mg	q12h	07 days	600 mg
Acute Pelvic Inflammatory Disease	400 mg	q12h	10-14 days	400 mg
Uncomplicated Cystitis due to E. coli or K. pneumoniae	200 mg	q12h	03 days	800 mg
Uncomplicated Cystitis due to other approved pathogens	200 mg	q12h	07 days	400 mg
Complicated UTI's	200 mg	q12h	10 days	400 mg
Prostatitis due to E.Coli	300 mg	q12h	06 weeks	600 mg

Antacids containing calcium, magnesium, or aluminum; sucralfate; divalent or trivalent cations such as iron; or multivitamins containing zinc; or Videx® (didanosine) should not be taken within the two-hour period before or within the twohour period after taking ofloxacin.

Patients with Impaired Renal Function:

Dosage should be adjusted for patients with a creatinine clearance less than or equal to 50 mL/min. After a normal initial dose, dosage should be adjusted as follows:

Table 3: Recommended Dose for Impaired Renal Function:

Creatinine Clearance	Maintenance Dose	Frequency
20-50 mL/min	The usual recommended unit	q24h
< 20 mL/min	Dose 1/2 the usual recommended unit dose	q24h

When only the serum creatinine is known, the following formula may be used to estimate creatinine clearance.

$$\text{Men: Creatinine clearance (mL/min)} = \frac{\text{Weight (kg) x (140-age)}}{\text{72 x serum creatinine (mg/dL)}}$$

Women: 0.85 x the value calculated for men.
The serum creatinine should represent a steady-state of renal function.

Patients with Cirrhosis:

The excretion of ofloxacin may be reduced in patients with severe liver function disorders (e.g., cirrhosis with or without ascites). A maximum dose of 400 mg of ofloxacin per day should therefore not be exceeded.

OVERDOSE

Information on overdosage with ofloxacin is limited. In the event of an acute overdose, the stomach should be emptied. The patient should be observed and appropriate hydration maintained. Ofloxacin is not efficiently removed by hemodialysis or peritoneal dialysis.

STORAGE/PRECAUTIONS: Store in a cool, dry and dark place between 15-30 °C. Keep all medicines out of the reach of children. To be used on the prescription of Registered Medical Practitioners only

PRESENTATION: OFLOSCOT Tablets are available in packing containing 10 Film coated tablets

خوراک: ڈاکٹر کی ہدایت کے مطابق۔

احتیاط: روشنی، نمی اور گرمی سے بچائیں۔ 15 سے 30 ڈگری سینٹی گریڈ کے درمیان محفوظ کریں۔
تمام ادویات بچوں کی پہنچ سے دور رکھیں۔ مستند ڈاکٹر کے نسخہ پر فروخت اور استعمال کریں۔

Complete Medical Information available only for doctors on request.

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