treated.

Hematopoietic:	anemia, leukopenia, leukocytosis, neutropenia, neutrophilia, increased band forms, lympho- cytopenia, eosinophilia, lymphocytosis, thrombocytopenia, thrombocytosis, elevated ESR
Hepatic:	elevated:alkaline phosphatase, AST (SGOT), ALT (SGPT)
Serum chemistry:	hyperglycemia, hypoglycemia, elevated creatinine, elevated BUN
Urinary:	glucosuria, proteinuria, alkalinuria, hyposthenuria, hematuria, pyuria

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 chewable/buffered tablets 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.

Drugs metabolized by Cytochrome P450 enzymes: Most quinolone antimicrobial drugs inhibit cytochrome P450 enzyme activity. This may result in a prolonged half-life for some drugs that are also metabolized by this system (e. g. , cyclosporine, theophylline/methylxanthines, warfarin) when co-administered with quinolones. The extent of this inhibition varies among different quinolones. *Non-steroidal anti-inflammatory drugs:* The concomitant administration of a non-steroidal anti-inflammatory drug with a quinolone, including ofloxacin, may increase the risk of CNS stimulation and convulsive seizures. *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 orits 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 (e. g. , insulin, glyburide/glibenclamide): 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.

STORAGE

Store below 30°C, in a dry place, protect from light.
To be dispensed on the prescription of a registered medical practitioner only.
Keep out of the reach of children.

AVAILABILITY:

10 film coated tablets in a blister pack.

CAUTION:

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر خشک جگہ پر رکھیں،
روشنی سے بچائیں۔ صرف رجسٹرڈ ڈاکٹر کے نسخے پر فروخت کریں۔
بچوں کی پہنچ سے دُور رکھیں۔

Manufactured by:
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QAR No. AW19-0493

Gyrex
(Ofloxacin)

10 Film Coated Tablets
For bacterial infections

گائرِیکس
(اوفلاکساسین)
۱۰ فلم بند گولیاں

COMPOSTION:

Each Film-Coated Tablet contains:
Ofloxacin . . . . . 200 mg

CLINICAL PHARMACOLOGY

PHARMACODYNAMIC PROPERTIES

Ofloxacin is a quinolone-carboxylic acid derivative with a wide range of antibacterial activity against both gram negative and gram positive organisms. It is active after oral administration. It inhibits bacterial DNA replication by blocking DNA topo-isomerases, in particular DNA gyrase.
Therapeutic doses of ofloxacin are devoid of pharmacological effects on the voluntary or autonomic nervous systems.
Microbiological results indicate that the following pathogens may be regarded as sensitive: Staphylococcus aureus (including methicillin resistant staphylococci), Staphylococcus epidermidis, Neisseria species, Escherichia coli, Citrobacter, Klebsiella, Enterobacter, Hafnia, Proteus (indole-negative and indole-positive strains), Haemophilus influenzae, Chlamydiae, Legionella, Gardnerella.
Variable sensitivity is shown by Streptococci, Serratia marcescens, Pseudomonas aeruginosa and Mycoplasmas.
Anaerobic bacteria (e.g. Fusobacterium species, Bacteroides species, Eubacterium species, Peptococci, Peptostreptococci) are normally resistant.
Gyrex is not active against Treponema pallidum.

PHARMACOKINETIC PROPERTIES

Ofloxacin is almost completely absorbed after oral administration. Maximal blood levels occur 1-3 hours after dosing and the elimination half-life is 4-6 hours. Ofloxacin is primarily excreted unchanged in the urine.
In renal insufficiency the dose should be reduced.
No clinically relevant interactions were seen with food and no interaction was found between ofloxacin and theophylline.

INDICATIONS

For the treatment of moderate to serious infections caused by susceptible strains of microorganisms. Ofloxacin should be prescribed on the basis of microbiological test results and microbiological susceptibility assessment. Lower respiratory tract infection, urinary tract infection, prostatitis, bone infection, skin and soft tissue infections including wound infection, intraabdominal infection including cholangitis and pelvic infections caused by susceptible microorganisms, respiratory infection in cystic fibrosis, in combination with other antituberculous drugs in pulmonary tuberculosis caused by resistant mycobacterial strains, sexually transmitted diseases except syphilis, shigellosis, salmonellosis, traveller's diarrhea, sepsis, bacteremia, infections in debilitated patients (e.g. in patients with tuberculosis, AIDS, etc.). In children only in case of serious life threatening infection (respiratory infection in cystic fibrosis, infections accompanying tumorous diseases).

DOSAGE AND ADMINISTRATION

General dosage recommendations: The dose of ofloxacin is determined by the type and severity of the infection. The dosage range for adults is 200mg to 800mg daily. Up to 400mg may be given as a single dose, preferably in the morning, larger doses should be given as two divided doses. Generally, individual doses are to be given at approximately equal intervals. Gyrex tablets should be swallowed with liquid; they should not be taken within two hours of magnesium/aluminium containing antacids, sucralfate, zinc or iron preparations since reduction of absorption of ofloxacin can occur.
Lower urinary tract infection: 200-400 mg daily.
Upper urinary tract infection: 200-400 mg daily increasing, if necessary, to 400 mg twice a day.
Lower respiratory tract infection: 400 mg daily increasing, if necessary, to 400 mg twice daily.
Uncomplicated urethral and cervical gonorrhoea: A single dose of 400 mg.
Non-gonococcal urethritis and cervicitis: 400 mg daily in single or divided doses.
Skin and soft tissue infections: 400 mg twice daily.
Impaired renal function: Following a normal initial dose, dosage should be reduced in patients with

impairment of renal function. When creatinine clearance is 20-50 ml/minute (serum creatinine 1.5-5.0 mg/dl) the dosage should be reduced by half (100-200 mg daily). If creatinine clearance is less than 20 ml/minute (serum creatinine greater than 5 mg/dl) 100 mg should be given every 24 hours. In patients undergoing haemodialysis or peritoneal dialysis, 100 mg should be given every 24 hours.
Impaired liver function: The excretion of ofloxacin may be reduced in patients with severe hepatic dysfunction.
Elderly: No adjustment of dosage is required in the elderly, other than that imposed by consideration of renal or hepatic function..
Children: Ofloxacin is not indicated for use in children or growing adolescents.
Duration of treatment: Duration of treatment is dependent on the severity of the infection and the response to treatment. The usual treatment period is 5–10 days except in uncomplicated gonorrhoea, where a single dose is recommended.
Treatment should not exceed 2 months duration, or as prescribed by the physician .

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 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 uncomplicated cystitis
- Acute sinusitis

CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients.
Ofloxacin should not be used in patients with a past history of tendonitis.
Ofloxacin, like other 4-quinolones, is contra-indicated in patients with a history of epilepsy or with a lowered seizure threshold. Ofloxacin is contra-indicated in children or growing adolescents, and in pregnant or breast-feeding women, since animal experiments do not entirely exclude the risk of damage to the cartilage of joints in the growing subject.
Patients with latent or actual defects in glucose-6-phosphate dehydrogenese activity may be prone to haemolytic reactions when treated with quinolone antibacterial agents.

WARNINGS

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.
Other serious and sometimes fatal events, some due to hypersensitivity, and some due to uncertain etiology, have been reported rarely in patients receiving therapy with quinolones, including ofloxacin. These events may be severe and generally occur following the administration of multiple doses. Clinical manifestations may include one or more of the following:

- fever, rash, or severe dermatologic reactions (e.g., toxic epidermal necrolysis, Stevens-Johnson syndrome);
- vasculitis; arthralgia; myalgia; serum sickness;
- allergic pneumonitis;
- interstitial nephritis; acute renal insufficiency or failure;
- hepatitis; jaundice; acute hepatic necrosis or failure;
- anemia, including hemolytic and aplastic; thrombocytopenia, including thrombotic thrombocytopenic purpura; leucopenia; granulocytosis; pancytopenia; and/or other hematologic abnormalities.

The drug should be discontinued immediately at the first appearance of skin rash, jaundice, or any other sign of hypersensitivity and supportive measures instituted.

Peripheral Neuropathy

Rare cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesias, hypoesthesias, dysesthesias and weakness have been reported in patients receiving quinolones, including ofloxacin. 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) has been reported with use of nearly all antibacterial agents, including ofloxacin tablets, 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.
If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

Tendon Effects

Ruptures of the shoulder, hand, Achilles tendon or other tendons that required surgical repair or resulted in prolonged disability have been reported in patients receiving quinolones, including ofloxacin. Postmarketing surveillance reports indicate that the risk is increased in patients receiving corticosteroids, especially the elderly. Ofloxacin should be discontinued if the patient experiences pain, inflammation, or rupture of a tendon. Patients should rest and refrain from exercise until the diagnosis of tendonitis or tendon rupture has been confidently excluded. Tendon rupture can occur during or after therapy with quinolones, including ofloxacin.
Ofloxacin has not been shown to be effective in the treatment of syphilis.
Antimicrobial agents used in high doses for short periods of time to treat gonorrhea may mask or delay the symptoms of incubating syphilis. All patients with gonorrhea should have a serologic test for syphilis at the time of diagnosis. Patients treated with ofloxacin for gonorrhea should have a follow-up serologic test for syphilis after three months and, if positive, treatment with an appropriate antimicrobial should be instituted.

ADVERSE EFFECTS

The following is a compilation of the data for ofloxacin based on clinical experience with both the oral and intravenous formulations. The incidence of drug-related adverse reactions in patients during Phase 2 and 3 clinical trials was 11%. Among patients receiving multiple-dose therapy, 4% discontinued ofloxacin due to adverse experiences.
In clinical trials, the following events were considered likely to be drug-related in patients receiving multiple doses of ofloxacin: nausea 3%, insomnia 3%, headache 1%, dizziness 1%, diarrhea 1%, vomiting 1%, rash 1%, pruritus 1%, external genital pruritus in women 1%, vaginitis 1%, dysgeusia 1%.
In clinical trials, the most frequently reported adverse events, regardless of relationship to drug, were: nausea 10%, headache 9%, insomnia 7%, external genital pruritus in women 6%, dizziness 5%, vaginitis 5%, diarrhea 4%, vomiting 4%.
In clinical trials, the following events, regardless of relationship to drug, occurred in 1 to 3% of patients:
Abdominal pain and cramps, chest pain, decreased appetite, dry mouth, dysgeusia, fatigue, flatulence, gastrointestinal distress, nervousness, pharyngitis, pruritus, fever, rash, sleep disorders, somnolence, trunk pain, vaginal discharge, visual disturbances, and constipation.
Additional events, occurring in clinical trials at a rate of less than 1%, regardless of relationship to drug, were:

Body as a whole:	asthenia, chills, malaise, extremity pain, pain, epistaxis
Cardiovascular System:	cardiac arrest, edema, hypertension, hypotension, palpitations, vasodilation
Gastrointestinal System:	dyspepsia
Genital/Reproductive System:	burning, irritation, pain and rash of the female genitalia; dysmenorrhea; menorrhagia; metrorrhagia
Musculoskeletal System:	arthralgia, myalgia
Nervous System:	seizures, anxiety, cognitive change, depression, dream abnormality, euphoria, hallucinations, paresthesia, syncope, vertigo, tremor, confusion
Nutritional/Metabolic:	thirst, weight loss
Respiratory System:	Respiratory arrest, cough, rhinorrhea
Skin/Hypersensitivity:	angioedema, diaphoresis, urticaria, vasculitis
Special Senses:	decreased hearing acuity, tinnitus, photophobia
Urinary System:	dysuria, urinary frequency, urinary retention

The following laboratory 1. 0% of patients receiving abnormalities appeared in multiple doses of ofloxacin. It is not known whether these abnormalities were caused by the drug or the underlying conditions being