Lee-flox 250 mg, 500 mg & 750 mg
Levofloxcin
Film coated tablets

Name of medicinal product

Lee-flox 250 mg, 500 mg and 750 mg Film Coated Tablet

Qualitative and quantitative composition

Active ingredient
Lee-Flox 250 mg: Levofloxacin hydrochloride 275.25 mg Eq. to 250 mg levofloxacin

Lee-Flox 500 mg: Levofloxacin hydrochloride 550.5 mg Eq. to 500 mg levofloxacin

Lee-Flox 750 mg: Levofloxacin hydrochloride 825.75 mg Eq. to 750 mg levofloxacin

Inactive ingredients
Lee-flox 250 mg: Lactose monohydrate, Croscarmellose sodium, Povidone K30, Magnesium stearate, Hydrpxypropyl methyl cellulose, Titanium dioxide, Talc powder, Polyethylene glycol 6000,
Lee-flox 500 mg : Lactose monohydrate, Croscarmellose sodium, Povidone K30, Magnesium stearate, Hydrpxypropyl methyl cellulose, Titanium dioxide, Talc powder, Polyethylene glycol 6000,
Lee-flox 750 mg : Lactose monohydrate, Croscarmellose sodium, Povidone K30, Magnesium stearate, Methocel, Titanium dioxide, Talc powder, Polyethylene glycol 6000, D&C Red no 30, Iron oxide red,

Pharmaceutical form
Lee-Flox 250 mg: White to off white round biconvex film coated tablets

Lee-Flox 500 mg: White to off white round biconvex film coated tablets

Lee-Flox 750 mg: Pink oblong biconvex film coated tablets

INDICATIONS AND CLINICAL USE

Lee-flox tablets are indicated for the treatment of adults with bacterial infections caused by susceptible strains of the designated microorganisms in the infections listed below.

-Upper Respiratory Tract
Acute sinusitis (mild to moderate) due to *Streptococcus pneumoniae, Haemophilus influenzae*, or *Moraxella (Branhamella) catarrhalis*.

Dr/Shaza 25/3/2024

Central Administration for Pharmaceutical care Approval Date: 25 / 3/2024 1st Revisor: Dr/Shaza
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"Restrict the use of Lee-flox to settings where no other treatment options exist, and the clinical presentation meets the diagnostic criteria for acute bacterial sinusitis."

-Lower Respiratory Tract
Acute bacterial exacerbations of chronic bronchitis (mild to moderate) due to Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae, Haemophilus parainfluenzae, or Moraxella (Branhamella) catarrhalis.

Community-acquired pneumonia (mild, moderate and severe infections) due to Staphylococcus aureus, Streptococcus pneumoniae (including penicillin-resistant strains), Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Moraxella (Branhamella) catarrhalis, Chlamydia pneumoniae, Legionella pneumophila, or Mycoplasma pneumonia.

Nosocomial pneumonia due to methicillin-susceptible Staphylococcus aureus, Pseudomonas aeruginosa, Serratia marcescens, Escherichia coli, Klebsiella pneumoniae, Haemophilus influenzae or Streptococcus pneumoniae. Adjunctive therapy should be used as clinically indicated. Where Pseudomonas aeruginosa is a documented or presumptive pathogen, combination therapy with an anti-pseudomonal β-lactam is recommended.

Lee-flox is not indicated for acute bronchitis.

Lee-flox should not be prescribed to patients with acute bacterial exacerbations of simple/uncomplicated chronic obstructive pulmonary disease (ie. patients who have chronic obstructive pulmonary disease without underlying risk factors)

-Skin and Skin Structure
Uncomplicated skin and skin structure infections (mild to moderate) due to *Staphylococcus aureus* or *Streptococcus pyogenes*.

Complicated skin and skin structure infections (mild to moderate), excluding burns, due to *Enterococcus faecalis*, methicillin-sensitive *Staphylococcus aureus, Streptococcus pyogenes, Proteus mirabilis*, or *Streptococcus agalactiae*.

-Urinary Tract
Complicated urinary tract infections (mild to moderate) due to *Enterococcus (Streptococcus) faecalis, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis*, or *Pseudomonas aeruginosa*
Uncomplicated urinary tract infections (mild to moderate) due to *Escherichia coli, Klebsiella pneumoniae* or *Staphylococcus saprophyticus*.

Acute pyelonephritis (mild to moderate) caused by *Escherichia coli*.

Chronic bacterial prostatitis due to *Escherichia coli, Enterococcus faecalis* or *Staphylococcus epidermidis*.

Appropriate culture and susceptibility tests should be performed before treatment in order to isolate and identify the organisms causing the infection, and to determine their susceptibility to levofloxacin. Therapy with Lee-flox may be initiated before the results of these tests are known; once results become available, appropriate therapy should be continued.

In cases of uncomplicated acute bacterial cystitis, limit the use of Lee-flox to circumstances where no other treatment options are available. A urine culture should be obtained prior to treatment to ensure levofloxacin susceptibility.

As with other drugs in this class, some strains of *Pseudomonas aeruginosa* may develop resistance fairly rapidly during treatment with Lee-flox. Culture and susceptibility testing performed periodically during therapy, will reveal not only the therapeutic effect of the antimicrobial agent, but also the possible emergence of bacterial resistance.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Lee-flox and other antibacterial drugs, Lee-flox should be used only to treat 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.

Geriatrics (≥65 years of age):
Drug absorption appears to be unaffected by age. Dose adjustment based on age alone is not necessary .

Pediatric Use (<18 years of age):
Safety and effectiveness in children under 18 years of age have not been established .

- Fluoroquinolones should be reserved for use in patients who have no other treatment options for acute bacterial sinusitis, (ABS), acute bacterial exacerbation of chronic bronchitis (ABECB), and uncomplicated urinary tract infections (UTI).

-Fluoroquinolones should not be used in the following indications:
- To treat infections that might get better without treatment or are not severe (such as throat infections);
- To treat non-bacterial infections, e.g. non-bacterial (chronic) prostatitis;
-For preventing traveller's diarrhoea or recurring lower urinary tract infections (urine infections that do not extend beyond the bladder);
To treat mild or moderate bacterial infections unless other antibacterial medicines commonly recommended for these infections cannot be used.

CONTRAINDICATIONS
Lee-flox is contraindicated in persons with a history of hypersensitivity to levofloxacin, quinolone antimicrobial agents, or to any components of this product.

Lee-flox is also contraindicated in persons with a history of tendinitis or tendon rupture associated with the use of any member of the quinolone group of antimicrobial agents.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Levofloxacin has been shown to prolong the QT interval of the electrocardiogram in some patients .
- Serious hypersensitivity and/or anaphylactic reactions have been reported in patients receiving quinolone therapy, including levofloxacin .
- Seizures may occur with quinolone therapy. Lee-flox should be used with caution in patients with known or suspected CNS disorders which may predispose to seizures or lower the seizure threshold .

- Fluoroquinolones, including-levofloxacin , may exacerbate muscle weakness in persons with myasthenia gravis. Avoid Lee-flox in patients with a known history of myasthenia gravis (see WARNINGS AND PRECAUTIONS, Musculoskeletal).
- Fluoroquinolones, including levofloxacin, have been associated with disabling and potentially persistent adverse reactions which to date include, but are not limited to: tendonitis, tendon rupture, peripheral neuropathy and neuropsychiatric effects.

General
The administration of levofloxacin increased the incidence and severity of osteochondrosis in immature rats and dogs. Other quinolones also produce similar erosions in the weight-bearing joints and other signs of arthropathy in immature animals of various species. Consequently, levofloxacin should not be used in pre-pubertal patients .

Although levofloxacin is soluble, adequate hydration of patients receiving levofloxacin should be maintained to prevent the formation of a highly concentrated urine. Crystalluria has been observed rarely in patients receiving other quinolones, when associated with high doses and an alkaline urine. Although crystalluria was not observed in clinical trials with levofloxacin, patients are encouraged to remain adequately hydrated.

As with any antimicrobial drug, periodic assessment of organ system functions, including renal, hepatic, and hematopoietic, is advisable during prolonged therapy (see ADVERSE REACTIONS).

Use of Lee-flox with other drugs may lead to drug-drug interactions (see DRUG INTERACTIONS, Drug-Drug Interactions).

Sexually Transmitted Diseases

Lee-flox is not indicated for the treatment of syphilis or gonorrhea. Levofloxacin is not 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 antimicrobial agents with limited or no activity against *Treponema pallidum* should have a follow- up serologic test for syphilis after 3 months.

Cardiovascular

QT Prolongation

Some quinolones, including levofloxacin, have been associated with prolongation of the QT interval on the electrocardiogram and infrequent cases of arrhythmia. During post-marketing surveillance, very rare cases of torsades de pointes have been reported in patients taking levofloxacin. These reports generally involved patients with concurrent medical conditions or concomitant medications that may have been contributory. The risk of arrhythmias may be reduced by avoiding concurrent use with other drugs that prolong the QT interval including macrolide antibiotics, antipsychotics, tricyclic antidepressants, Class IA (e.g., quinidine, procainamide) or Class III (e.g., amiodarone, sotalol) antiarrhythmic agents, and cisapride. In addition, use of levofloxacin in the presence of risk factors for torsades de pointes such as hypokalemia, significant bradycardia, cardiomyopathy, patients with myocardial ischemia, and patients with congenital prolongation of the QT interval should be avoided .

Aortic Aneurysm and Aortic Dissection

Aortic aneurysm and dissection, and heart valve regurgitation/incompetence:
Epidemiologic studies report an increased risk of aortic aneurysm and dissection, particularly in elderly patients, and of aortic and mitral valve regurgitation after intake of fluoroquinolones.
Cases of aortic aneurysm anddissection, sometimes complicated by rupture (including fatal ones), and of regurgitation/incompetence of any of the heart valves have been reported in patients receiving fluoroquinolones .
Therefore, fluoroquinolones should only be used after a careful benefit-risk assessment and after consideration of other therapeutic options in patients with positive family history of aneurysm disease or congenital heart valve disease, or in patients diagnosed with pre-existing aortic aneurysm and/or dissection or heart valve disease, or in presence of other risk factors or conditions predisposing
- For both aortic aneurysm and dissection and heart valve regurgitation/incompetence(e.g. connective tissue disorders such as Marfan syndrome or Ehlers-Danlossyndrome, Turner syndrome, Behçet s disease,hypertension, rheumatoid arthritis) or additionally
- For aortic aneurysm and dissection (e.g. vascular disorders such as Takayasu arteritis or giant cell arteritis, or known atherosclerosis, or Sjögren's syndrome)or additionally
- For heart valve regurgitation/incompetence (e.g. infective endocarditis).
The risk of aortic aneurysm and dissection, and their rupture may also be increased in patients treated

concurrently with systemic corticosteroids.
Patients should be advised to seek immediate medical attention in case of acute dyspnoea, new onset of heart palpitations, or development of oedema of the abdomen or lower extremities.

Therefore, fluoroquinolones should only be used after careful benefit- risk assessment and after consideration of other therapeutic options in patients with positive family history of aneurysm disease, or in patients diagnosed with pre-existing aortic aneurysm and/or aortic dissection, or in presence of other risk factors or conditions predisposing for aortic aneurysm and dissection (e.g. Marfan syndrome, vascular Ehlers- Danlos syndrome, Takayasu arteritis, giant cell arteritis, Behcet's disease, hypertension, known atherosclerosis).
In case of sudden abdominal, chest or back pain, patients should be advised to immediately consult a physician in an emergency department.

Endocrine and Metabolism

Blood Glucose Disturbances

Fluoroquinolones, including levofloxacin, have been associated with disturbances of blood glucose, including symptomatic hyperglycemia and hypoglycemia, usually in diabetic patients receiving concomitant treatment with an oral hypoglycemic agent (e.g., glyburide) or with insulin. In these patients, careful monitoring of blood glucose is recommended. Severe cases of hypoglycemia resulting in coma or death have been reported. If a hypoglycemic reaction occurs, discontinue Lee-flox immediately and initiate appropriate therapy.

Disturbances of blood glucose, including symptomatic hyper- and hypoglycemia, have been reported with the use of quinolones, including levofloxacin. In patients treated with levofloxacin, some of these cases were serious. Blood glucose disturbances were usually in diabetic patients receiving concomitant treatment with an oral hypoglycemic agent (e.g., glyburide/glibenclamide) and/or with insulin. In these patients, careful monitoring of blood glucose is recommended. If a hypoglycemic reaction occurs in a patient being treated with Lee-flox, discontinue Lee-flox immediately and initiate appropriate therapy. Serious hypoglycemia and hyperglycemia have also occurred in patients without a history of diabetes .

Hypoglycemic coma has been observed in diabetic patients with the use of levofloxacin. Fatal outcomes have been reported. All cases of hypoglycemic coma had multiple confounding factors; a temporal relationship with the use of levofloxacin was identified (onset of altered consciousness occurred within 3 days in most cases). Caution should be exercised when using Lee-flox in diabetic patients taking concomitant treatment with an oral hypoglycemic agent and/or insulin, especially those who are elderly or who have renal impairment .

Gastrointestinal

***Clostridium difficile*-associated disease**

Clostridium difficile-associated disease (CDAD) has been reported with use of many antibacterial agents, including levofloxacin. CDAD may range in severity from mild diarrhea to fatal colitis. It is important to consider this diagnosis in patients who present with diarrhea or symptoms of colitis, pseudomembranous colitis, toxic megacolon, or perforation of the colon subsequent to the administration of any antibacterial agent. CDAD has been reported to occur over 2 months after the

administration of antibacterial agents.

Treatment with antibacterial agents may alter the normal flora of the colon and may permit overgrowth of *Clostridium difficile*. *C. difficile* produces toxins A and B, which contribute to the development of CDAD. CDAD may cause significant morbidity and mortality. CDAD can be refractory to antimicrobial therapy.

If the diagnosis of CDAD is suspected or confirmed, appropriate therapeutic measures should be initiated. Mild cases of CDAD usually respond to discontinuation of antibacterial agents not directed against *Clostridium difficile*. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial agent clinically effective against *Clostridium difficile*. Surgical evaluation should be instituted as clinically indicated since surgical intervention may be required in certain severe cases (see ADVERSE REACTIONS).

Hepatic

Very rare post-marketing reports of severe hepatotoxicity (including acute hepatitis and fatal events) have been received for patients treated with levofloxacin. No evidence of serious drug- associated hepatotoxicity was detected in clinical trials of over 7000 patients. Severe hepatotoxicity generally occurred within 14 days of initiation of therapy and most cases occurred within 6 days. Most cases of severe hepatotoxicity were not associated with hypersensitivity.
The majority of fatal hepatotoxicity reports occurred in patients 65 years of age or older and most were not associated with hypersensitivity. Lee-flox should be discontinued immediately if the patient develops signs and symptoms of hepatitis .

Hypersensitivity

Serious and occasionally fatal hypersensitivity and/or anaphylactic reactions have been reported in patients receiving therapy with quinolones, including levofloxacin. 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. Lee-flox 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 (see ADVERSE REACTIONS).

Serious and sometimes fatal events, some due to hypersensitivity and some due to uncertain etiology, have rarely been reported in patients receiving therapy with quinolones, including levofloxacin. 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, including acute hepatitis; jaundice; acute hepatic necrosis or failure; anemia, including hemolytic and aplastic; thrombocytopenia, including thrombotic thrombocytopenic purpura; leukopenia; agranulocytosis; pancytopenia; and/or other hematologic abnormalities. The administration of Lee-flox

should be discontinued immediately, at the first appearance of a skin rash or any other sign of hypersensitivity, and supportive measures instituted (see ADVERSE REACTIONS).

Musculoskeletal

Tendinitis

Rupture of the shoulder, hand and Achilles tendons that required surgical repair or resulted in prolonged disability have been reported in patients receiving quinolones, including levofloxacin. Lee-flox 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 tendinitis or tendon rupture has been confidently excluded. The risk of developing fluoroquinolone-associated tendinitis and tendon rupture is further increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs,-in patients receiving daily doses of 1000 mg 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. Lee-flox 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 (see adverse reactions).

Lee-flox should not be used in patients with a history of tendon disease/disorder related to previous quinolone treatment (see contraindications).

Myasthenia Gravis

Fluoroquinolones have neuromuscular blocking activity and may exacerbate muscle weakness in persons with myasthenia gravis. Postmarketing serious adverse events, including deaths and requirement for ventilatory support, have been associated with fluoroquinolone use (including levofloxacin) in persons with myasthenia gravis. Avoid levofloxacin in patients with a known history of myasthenia gravis (see ADVERSE REACTIONS, Post-Market Adverse Drug Reactions).

Neurologic

CNS and Psychiatric Effects

Convulsions, toxic psychoses and increased intracranial pressure (including pseudotumor cerebri) have been reported in patients receiving quinolones, including levofloxacin. Quinolones including levofloxacin, may also cause central nervous system stimulation which may lead to tremors, restlessness, anxiety, lightheadedness, dizziness, confusion and hallucinations, paranoia, depression, nightmares, insomnia, and rarely, suicidal thoughts or acts. These reactions may occur following the first dose. If these reactions occur in patients receiving Lee-flox, the drug should be discontinued and appropriate measures instituted. As with all quinolones, Lee-flox should be used with caution in patients with a known or suspected CNS disorder that may predispose to seizures or lower the seizure threshold (e.g., severe cerebral arteriosclerosis, epilepsy), or in the presence of other risk factors that may predispose to seizures or lower the seizure threshold (e.g., alcohol abuse, certain drug therapies such as NSAIDs and

theophylline, renal dysfunction). Lee-flox should be used with caution in patients with unstable psychiatric illness (see DRUG INTERACTIONS and ADVERSE REACTIONS).

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 levofloxacin. Symptoms may occur soon after initiation of treatment and may be irreversible. Lee-flox should be discontinued immediately 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.

Central Nervous System Effects

Psychiatric Adverse Reactions

Fluoroquinolones, including levofloxacin, have been associated with an increased risk of psychiatric adverse reactions, including: toxic psychoses, hallucinations, or paranoia; depression, or suicidal thoughts; anxiety, agitation, restlessness, or nervousness; confusion, delirium, disorientation, or disturbances in attention; insomnia or nightmares; and memory impairment.

Cases of attempted or completed suicide have been reported, especially in patients with a medical history of depression, or an underlying risk factor for depression. These reactions may occur following the first dose. If these reactions occur in patients receiving Lee-flox, discontinue Lee-flox and institute appropriate measures.

Central Nervous System Adverse Reactions

Fluoroquinolones, including levofloxacin, have been associated with an increased risk of seizures (convulsions), increased intracranial pressure (including pseudotumor cerebri), tremors, and light-headedness. As with other fluoroquinolones, Lee-flox should be used with caution in patients with a known or suspected central nervous system (CNS) disorder that may predispose them to seizures or lower the seizure threshold (e.g., severe cerebral arteriosclerosis, epilepsy) or in the presence of other risk factors that may predispose them to seizures or lower the seizure threshold (e.g., certain drug therapy, renal dysfunction). If these reactions occur in patients receiving Lee-flox, discontinue Lee-flox immediately and institute appropriate measures.

Ophthalmologic

Vision Disorders

Consult an eye specialist if vision disorder occurs in association with the use of Lee-flox.

Renal

Safety and efficacy of levofloxacin in patients with impaired renal function (creatinine clearance ≤ 80 mL/min) have not been studied. Since levofloxacin is known to be substantially excreted by the kidney, the risk of toxic reactions to this drug may be greater in patients with impaired renal function. The potential effects of levofloxacin associated with possible increased serum/tissue levels in renal impaired patients, such as effect on QTc interval, have not been studied.

Adjustment of the dosage regimen may be necessary to avoid the accumulation of levofloxacin due to

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decreased clearance. Careful clinical observation and appropriate laboratory studies should be performed prior to and during therapy, since elimination of levofloxacin may be reduced. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection and it may be useful to monitor renal function. Administer Lee-flox with caution in the presence of renal insufficiency .

Skin

Phototoxicity

Moderate to severe phototoxicity reactions have been observed in patients exposed to direct sunlight or ultraviolet (UV) light while receiving drugs in this class. Excessive exposure to sunlight or UV light should be avoided. However, in clinical trials with levofloxacin, phototoxicity has been observed in less than 0.1% of patients. Therapy should be discontinued if phototoxicity (e.g., skin eruption) occurs.

Susceptibility/Resistance

Development of Drug Resistant Bacteria

Prescribing Lee-flox in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and risks the development of drug-resistant bacteria.

Special Populations

The safety and efficacy of levofloxacin in children, adolescents (under the age of 18 years), pregnant women, and nursing mothers have not been established.

Pregnant Women: There are no adequate and well-controlled studies in pregnant women. Lee-flox should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus

Nursing Women: Levofloxacin has not been measured in human milk. Based upon data from ofloxacin, it can be presumed that levofloxacin can be excreted in human milk. Because of the potential for serious adverse reactions from levofloxacin 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

Pediatrics (<18 years of age): Lee-flox is not indicated for the treatment of patients younger than 18 years of age. Quinolones, including levofloxacin, cause arthropathy in juvenile animals of several species The incidence of protocol-defined musculoskeletal disorders in a prospective long-term surveillance study was higher in children treated for approximately 10 days with levofloxacin than in children treated with non- fluoroquinolone antibiotics for approximately 10 days (see ADVERSE REACTIONS).

Geriatrics (≥65 years of age): The pharmacokinetic properties of levofloxacin in younger adults and elderly adults do not differ significantly when creatinine clearance is taken into consideration. However, since the drug is known to be substantially excreted by the kidney, the risk of toxic reactions to this drug may be greater in patients with impaired renal function.

Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection. It may also be useful to monitor renal function.

Elderly patients may be more susceptible to drug-associated effects on the QT interval (see warnings and precautions, Cardiovascular).

Geriatric patients are at increased risk for developing severe tendon disorders including tendon rupture when being treated with a fluoroquinolone such as levofloxacin. This risk is further increased in patients receiving concomitant corticosteroid therapy (see WARNINGS AND PRECAUTIONS, Musculoskeletal).

Severe and sometimes fatal cases of hepatotoxicity have been reported post-marketing in association with levofloxacin. The majority of fatal hepatotoxicity reports occurred in patients 65 years of age or older and most were not associated with hypersensitivity (see WARNINGS AND PRECAUTIONS, Hepatic).

Effects on Ability to Drive and Use Machines
Neurologic adverse effects such as dizziness and lightheadedness may occur. Therefore, patients should know how they react to Lee-flox before operating an automobile or machinery or engaging in other activities requiring mental alertness and coordination.

ADVERSE REACTIONS

Adverse Drug Reaction Overview
In clinical trials, the most frequently reported adverse drug reactions occurring in > 3% of the study population were nausea, headache, diarrhea, insomnia, dizziness and constipation.

Serious and otherwise important adverse drug reactions are discussed in greater detail in other sections (see warnings and precautions).

Clinical Trial Adverse Drug Reactions
Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

The data described below reflect exposure to levofloxacin in 7537 patients in 29 pooled Phase III clinical trials. The population studied had a mean age of 49.6 years (74.2% of the population was < 65 years), 50.1% were male, 71.0% were Caucasian and 18.8% were Black. Patients were treated with levofloxacin for a wide variety of infectious diseases (See INDICATIONS AND CLINICAL USE). Treatment duration was usually 3-14 days, the mean number of days on therapy was 9.6 days and the mean number of doses was 10.2. Patients received levofloxacin doses of 750 mg once daily, 250 mg once daily, or 500 mg once or twice daily. The overall incidence, type and distribution of adverse reactions were similar in patients receiving levofloxacin doses of 750 mg once daily, 250 mg once daily, and 500 mg once or twice daily.

Adverse reactions (characterized as likely related to drug-therapy) occurring in ≥1% of

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levofloxacin-treated patients are shown in Table 1.1 below.

Table 1.1: Common (≥1%) Adverse Reactions Reported in Clinical Trials with Levofloxacin

System/Organ Class	Adverse Reaction	% (N=7537)
Infections and Infestations	Moniliasis	1
Psychiatric Disorders	Insomnia	4[a]
Nervous System Disorders	Headache	6
	dizziness	3
Respiratory, Thoracic and Mediastinal	Dyspnea	1
Gastrointestinal Disorders	nausea	7
	diarrhea	5
	constipation	3
	abdominal pain	2
	vomiting	2
	dyspepsia	2
Skin and Subcutaneous Tissue Disorders	rash	2
	pruritus	1
Reproductive System and Breast Disorders	Vaginitis	1[b]
General Disorders and Administration Site Conditions	edema	1
	injection site reaction	1
	chest pain	1

[a] N = 7274
[b] N = 3758 (women)

Less Common Clinical Trial Adverse Drug Reactions (<1%)
Less common adverse reactions occurring in 0.1 to <1% of levofloxacin-treated patients are shown in Table 1.2 below.

Table 1.2: Less Common (0.1 to <1%) Adverse Reactions Reported in Clinical Trials with

Levofloxacin

System/Organ Class	Adverse Reaction
Infections and Infestations	genital moniliasis
Blood and Lymphatic System Disorders	anemia, thrombocytopenia, granulocytopenia
Immune System Disorders	allergic reaction
Metabolism and Nutrition	Hyperglycemia, hypoglycemia, hyperkalemia
Psychiatric Disorders	Agitation, confusion, depression, hallucination, Anxiety, Depression, suicidal thoughts & mental health problems. nightmare[a], sleep disorder[a], anorexia, abnormal dreaming[a]
Nervous System Disorders	Tremor, convulsions, paresthesia, vertigo, hypertonia, hyperkinesias, abnormal gait somnolence[a], syncope, Peripheral Neuropathy.
Respiratory, Thoracic and Mediastinal	epistaxis
Cardiac Disorders	cardiac arrest, palpitation, ventricular tachycardia, ventricular arrhythmia
Vascular Disorders	phlebitis
Gastrointestinal Disorders	gastritis, stomatitis, pancreatitis, esophagitis, gastroenteritis, glossitis, pseudomembranous/ *C.difficile* colitis
Hepatobiliary Disorders	abnormal hepatic function, increased hepatic enzymes, increased alkaline phosphatase
Skin and Subcutaneous Tissue Disorders	urticaria
Musculoskeletal and Connective Tissue	Arthralgia, myalgia, skeletal pain Tendinitis ,Joint Pain.
Renal and Urinary Disorders	abnormal renal function, acute renal failure

[a] N = 7274

Rare (<0.1%) adverse reactions from Phase III studies include dyspnea and rash maculo-papular.

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In clinical trials using multiple-dose therapy, ophthalmologic abnormalities, including cataracts and multiple punctate lenticular opacities, have been noted in patients undergoing treatment with other quinolones. The relationship of the drugs to these events is not presently established.

Crystalluria and cylindruria have been reported with other quinolones.

Cases of aortic aneurysm and dissection, sometimes complicated by rupture (including fatal ones), and of regurgitation/incompetence of any of the heart valves have been reported in patients receiving fluoroquinolones.

Abnormal Hematologic and Clinical Chemistry Findings

Laboratory abnormalities seen in > 2% of patients receiving multiple doses of levofloxacin: decreased glucose 2.1%

It is not known whether this abnormality was caused by the drug or the underlying condition being treated.

Pediatric Data

In a group of 1534 pediatric patients (6 months to 16 years of age) treated with levofloxacin for respiratory infections, children 6 months to 5 years of age received 10 mg/kg of levofloxacin twice a day for approximately 10 days and children greater than 5 years of age received 10 mg/kg to a maximum of 500 mg of levofloxacin once a day for approximately 10 days. The adverse reaction profile was similar to that reported in adult patients. Vomiting and diarrhea were reported more frequently in children than reported in adults. However, the frequency of vomiting and diarrhea was similar in levofloxacin-treated and non-fluoroquinolone antibiotic comparator-treated children.

A subset of 1340 of these children treated with levofloxacin for approximately 10 days was enrolled in a prospective, long-term, surveillance study to assess the incidence of protocol- defined musculoskeletal disorders (arthralgia, arthritis, tendinopathy, gait abnormality) during 60 days and 1 year following the first dose of levofloxacin.

During the 60-day period following the first dose, the incidence of protocol-defined musculoskeletal disorders was greater in levofloxacin-treated children than in non- fluoroquinolone antibiotic comparator-treated children (2.1% vs. 0.9%, respectively [p=0.038]). In 22/28 (78%) of these children, reported disorders were characterized as arthralgia. A similar observation was made during the one-year period, with a greater incidence of protocol-defined musculoskeletal disorders in levofloxacin-treated children than in non-fluoroquinolone antibiotic comparator-treated children (3.4% vs. 1.8%, respectively [p=0.025]). The majority of these disorders occurring in children treated with levofloxacin were mild and resolved within 7 days. Disorders were moderate in 8 children and mild in 35 (76%) children.

Post-Market Adverse Drug Reactions

Table 1.3 lists adverse reactions that have been identified during post-approval use of levofloxacin.

Because these reactions are reported voluntarily from a population of uncertain size, reliably estimating their frequency or establishing a causal relationship to drug exposure is not always possible.

Table 1.3: Post-Marketing Reports of Adverse Drug Reactions

System Organ Class	Adverse Reaction
Blood and Lymphatic System Disorders	pancytopenia, aplastic anemia, leucopenia, hemolytic anemia, eosinophilia, thrombocytopenia including thrombotic thrombocytopenic purpura, agranulocytosis
Immune System Disorders	hypersensitivity reactions, sometimes fatal including: anaphylactic/anaphylactoid reactions, anaphylactic shock, angioneurotic edema, serum sickness
Psychiatric Disorders	psychosis, paranoia, isolated reports of suicide attempt and suicidal ideation
Nervous System Disorders	anosmia, ageusia, parosmia, dysgeusia, peripheral neuropathy (may be irreversible), isolated reports of encephalopathy, abnormal EEG, dysphonia, exacerbation of myasthenia gravis, amnesia, pseudotumor cerebri
Eye Disorders	uveitis, vision disturbance (including diplopia), visual acuity reduced, vision blurred, scotoma
Ear and Labyrinth	hypoacusis, tinnitus
Cardiac Disorders	isolated reports of torsades de pointes, electrocardiogram QT prolonged, tachycardia
Vascular Disorders	vasodilation, vasculitis, DIC
Respiratory, Thoracic and	isolated reports of allergic pneumonitis, interstitial pneumonia, laryngeal edema, apnea
Hepatobiliary Disorders	hepatic failure (including fatal cases), hepatitis, jaundice, hepatic
Skin and Subcutaneous Tissue Disorders	bullous eruptions to include: Stevens-Johnson Syndrome, toxic epidermal necrolysis, erythema multiforme, photosensitivity/phototoxicity reaction, leukocytoclastic vasculitis
Musculoskeletal and Connective Tissue	tendon rupture, muscle injury (including rupture), rhabdomyolysis, myositis, myalgia
Renal and Urinary Disorders	interstitial nephritis, nephrosis, glomerulonephritis
General Disorders and Administration Site	multi-organ failure, pyrexia, rash
Investigations	prothrombin time prolonged, international normalized ratio (INR) prolonged, muscle enzymes increased (CPK)

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DRUG INTERACTIONS

Overview

Levofloxacin undergoes limited metabolism in humans and is primarily excreted as unchanged drug in the urine. The P450 system is not involved in the levofloxacin metabolism, and is not affected by levofloxacin. Levofloxacin is unlikely to alter the pharmacokinetics of drugs metabolized by these enzymes. Disturbances of blood glucose have been reported in patients treated concomitantly with levofloxacin and an antidiabetic agent. Therefore, careful monitoring of blood glucose is recommended when these agents, including levofloxacin, are co-administered. As with all other quinolones, iron and antacids significantly reduced bioavailability of levofloxacin.

Drug-Drug Interactions

Table 1.4: Established or Potential Drug-Drug Interactions

Proper name	Ref	Effect	Clinical comment
Antidiabic Agents	C	Disturbances of blood glucose, including hyperglycemia and hypoglycemia, have been reported in patients treated concomitantly with levofloxacin and an antidiabetic agent. Some of these cases were serious including hypoglycemic coma.	Careful monitoring of blood glucose is recommended when these agents, including levofloxacin, are co-administered.
Antacids, Sucralfate, Metal Cations, Multi-Vitamins	T	**Tablets:** Due to the chelation of levofloxacin by multivalent cations, concurrent administration of levofloxacin tablets with antacids containing calcium, magnesium, or aluminum, as well as sucralfate, metal cations such as iron, multi- vitamin preparations with zinc, or any products containing any of these components may interfere with the gastrointestinal absorption of levofloxacin, resulting in systemic levels considerably lower than desired.	These agents should be taken at least 2 hours before or 2 hours after levofloxacin tablet administration.

Cyclosporine	CT	No significant effect of levofloxacin on the peak plasma concentrations, AUC, and other disposition parameters for cyclosporine was detected in a clinical study involving healthy volunteers. However, elevated serum levels of cyclosporine have been reported in the patient population when co-administered with some other quinolones. Levofloxacin Cmax and ke were slightly lower, while Tmax and t½ were slightly longer in the presence of cyclosporine, than those observed in other studies without concomitant medication. The differences, however, are not considered to be clinically significant.	No dosage adjustment is required for levofloxacin or cyclosporine when administered concomitantly.
Digoxin	CT	No significant effect of levofloxacin on the peak plasma concentrations, AUC, and, other disposition parameters for digoxin was detected in a clinical study involving healthy volunteers. Levofloxacin absorption and disposition kinetics were similar in the presence or absence of digoxin.	No dosage adjustment for levofloxacin or digoxin is required when administered concomitantly. Digoxin levels should be closely monitored in patients receiving concomitant therapy with digoxin.
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	T	Although not observed with levofloxacin in clinical trials, some quinolones have been reported to have proconvulsant activity that is exacerbated with concomitant use of NSAIDs.	The concomitant administration of a non-steroidal anti-inflammatory drug with a quinolone, including levofloxacin, may increase the risk of CNS stimulation and convulsive seizures
Probenecid and Cimetidine	CT	No significant effect of probenecid or cimetidine on the rate and extent of levofloxacin absorption was observed in a clinical study involving healthy volunteers. The AUC and t½ of levofloxacin were 27-38% and 30% higher, respectively, while CL/F and Clr were 21-35% lower during concomitant treatment with probenecid or cimetidine compared to levofloxacin alone.	.No dosage adjustment for levofloxacin is required when administered concomitantly with probenecid or cimetidine except dosage adjustment for levofloxacin may be required based on the renal function of the patient.

Theophylline	CT/T	No significant effect of levofloxacin on the plasma concentrations, AUC, and other disposition parameters for theophylline was detected in a clinical study involving 14 healthy volunteers. Similarly, no apparent effect of theophylline on levofloxacin absorption and disposition was observed. However, concomitant administration of other quinolones with theophylline has resulted in prolonged elimination, elevated serum theophylline levels, and a subsequent increase in the risk of theophylline-related adverse reactions in the patient population.	Theophylline levels should be closely monitored, and theophylline dosage adjustments made if appropriate, when levofloxacin is co-administered. Adverse reactions, including seizures, may occur with or without an elevation in serum theophylline level.
Warfarin	T	Certain quinolones, including levofloxacin, may enhance the effects of oral anticoagulant warfarin or its derivatives.	When these products are administered concomitantly, prothrombin time, International Normalized Ratio (INR), or other suitable coagulation tests should be
Zidovudine	CT	Levofloxacin absorption and disposition in HIV- infected subjects, with or without concomitant zidovudine treatment, were similar. The effect of levofloxacin on zidovudine pharmacokinetics has not been studied.	No dosage adjustment for levofloxacin appears to be required when co-administered with zidovudine.

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

Drug-Food Interactions

Lee-flox may be taken with or without food.

Drug-Herb Interactions

Interactions with herbal products have not been established.

Drug-Laboratory Interactions

Some quinolones, including levofloxacin, 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.

DOSAGE AND ADMINISTRATION

Dosing Considerations

The dosage of levofloxacin tablets for patients with normal renal function (i.e., ClCr > 80 mL/min) is described in the following dosing chart. For patients with altered renal function (i.e., ClCr ≤ 80 mL/min),

Recommended Dose and Dosage Adjustment

Patients with Normal Renal Function

Infection*	Dose	Freq.	Duration
Acute Bacterial Exacerbation of Chronic Bronchitis	500 mg 750 mg	q24 h	7 days 5 days
Comm.-Acquired Pneumonia	500 mg 750 mg**	q24h q24h	7-14 days (10-14 days for severe infections) 5 days
Sinusitis	500 mg 750 mg***	q24 h	10-14 days 5 days
Nosocomial Pneumonia	750 mg	q24h	7-14 days
Uncomplicated SSSI	500 mg	q24h	7-10 days
Complicated SSSI	750 mg	q24h	7-14 days
Chronic Bacterial Prostatitis	500 mg	q24h	28 days
Complicated UTI	250 mg 750 mg‡	q24 h	10 days 5 days
Acute Pyelonephritis	250 mg 750 mg	q24 h	10 days 5 days
Uncomplicated UTI	250 mg	q24h	3 days

* DUE TO THE DESIGNATED PATHOGENS (see INDICATIONS AND CLINICAL USE).

** Efficacy of this alternative regimen has only been documented for infections caused by penicillin-susceptible Streptococcus pneumoniae, Haemophilus influenzae, Haemophilus parainfluenzae, Mycoplasma pneumoniae, Chlamydia pneumoniae, and Legionella pneumophila.

*** The efficacy of a regimen of 750 mg daily for 5 days has been demonstrated to be non-inferior to a regimen of 500 mg daily for 10 days. The 750 mg daily 5-day regimen has not been compared to a regimen of 500 mg daily for 11-14 days.

‡ The efficacy of this alternative regimen has been documented for infections caused by Escherichia coli, Klebsiella pneumoniae, and Proteus mirabilis. Efficacy against infections caused by Enterococcus faecalis, Enterobacter cloacae, or Pseudomonas aeruginosa has not been demonstrated with this regimen.

Patients with Impaired Renal Function

On the basis of the altered levofloxacin disposition pharmacokinetics in subjects with impaired renal function, dose adjustment is recommended for patients with impaired renal function as given below

Dosing recommendations for renally impaired patients are based on data collected from a clinical safety

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and pharmacokinetic study in renally impaired patients treated with a single 500 mg oral dose of levofloxacin. There is no clinical experience available in this patient population for the 250 mg dose or 750 mg dose. Pharmacokinetic modelling was used to determine a recommended dosing regimen which would provide equivalent drug exposures for which clinical efficacy has been demonstrated. The potential effects of levofloxacin associated with possible increased serum/tissue levels in renal impaired patients, such as effect on QTc interval, have not been studied.

Renal Status	Initial Dose	Subsequent Dose
Acute Sinusitis/Acute Bacterial Exacerbation of Chronic Bronchitis/Community Acquired Pneumonia/Uncomplicated SSSI/Chronic Bacterial Prostatitis		
ClCr from 50 to 80 mL/min	No dosage adjustment required	
ClCr from 20 to 49 mL/min	500 mg	250 mg q24h
ClCr from 10 to 19 mL/min	500 mg	250 mg q48h
Hemodialysis	500 mg	250 mg q48h
CAPD	500 mg	250 mg q48h
Complicated UTI/Acute Pyelonephritis		
ClCr ≥20 mL/min	No dosage adjustment required	
ClCr from 10 to 19 mL/min	250 mg	250 mg q48h
Complicated SSSI/Nosocomial Pneumonia/Community Acquired Pneumonia/Acute Bacterial Exacerbation of Chronic Bronchitis/Acute Sinusitis/Complicated UTI/Acute Pyelonephritis		
ClCr from 50 to 80 mL/min	No dosage adjustment required	
ClCr from 20 to 49 mL/min	750 mg	750 mg q48h
ClCr from 10 to 19 mL/min	750 mg	500 mg q48h
Hemodialysis	750 mg	500 mg q48h
CAPD	750 mg	500 mg q48h
Uncomplicated UTI	No dosage adjustment required	

ClCr = creatinine clearances
CAPD = continuous ambulatory peritoneal dialysis

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

Men: Creatinine Clearance (mL/min) = Weight (kg) x (140- age) x 1.2 / serum creatinine (mcmol/L)

Women: 0.85 x the value calculated for men.

The serum creatinine should represent a steady state of renal function.

Missed Dose

More than the prescribed dose of Lee-flox should not be taken, even if a dose is missed.

Administration

Lee-flox can be administered without regard to food. Doses should be administered at least 2 hours before or 2 hours after antacids containing calcium, magnesium, aluminum, sucralfate, metal

cations such as iron, multi-vitamin preparations with zinc, or products containing any of these components.
Take the tablet as a whole (not divided into two equal doses).

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

In the event of an acute overdosage, activated charcoal may be administered to aid in the removal of unabsorbed drug. General supportive measures are recommended. The patient should be observed, including ECG monitoring and appropriate hydration maintained. Treatment should be supportive. Levofloxacin is not efficiently removed by hemodialysis or peritoneal dialysis.

Reporting side effects:
Reporting suspected adverse reactions after authorization of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions via (see details below)
Human Pharmacovigilance Department – Egyptian Pharmaceutical Vigilance Center (EPVC)-Egyptian Drug Authority (EDA)
21 Abd Elaziz Al Souad st. – Manial El-Roda – Cairo, PO Box: 11451
Website: www.epvc.gov.eg
e-mail: pv.followup@edaegypt.gov.eg

ACTION AND CLINICAL PHARMACOLOGY
Mechanism of Action
Levofloxacin is a synthetic broad-spectrum antibacterial agent for oral administration and intravenous administration.

Levofloxacin is the L-isomer of the racemate, ofloxacin, a quinolone antibacterial agent. The antibacterial activity of ofloxacin resides primarily in the L-isomer. The mechanism of action of levofloxacin and other quinolone antibacterials involves inhibition of bacterial topoisomerase II (DNA gyrase) and topoisomerase IV. Topoisomerases are essential in controlling the topological state of DNA, and are vital for DNA replication, transcription, repair and recombination.

Fluoroquinolones, including levofloxacin, differ in chemical structure and mode of action from other classes of antimicrobial agents, such as β-lactam antibiotics, aminoglycosides, and macrolides. Therefore, microorganisms resistant to these latter classes of antimicrobial agents may be susceptible to fluoroquinolones. For example, β-lactamase production and alterations in penicillin-binding proteins have no effect on levofloxacin activity. Conversely, microorganisms resistant to fluoroquinolones may be susceptible to other classes of antimicrobial agents.

Pharmacokinetics

Absorption:

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Oral
Levofloxacin is rapidly and essentially completely absorbed after oral administration. Peak plasma concentrations are usually attained 1 to 2 hours after oral dosing. The absolute bioavailability of a 500 mg tablet and a 750 mg tablet of levofloxacin is approximately 99% in both cases, demonstrating complete oral absorption of levofloxacin.
Levofloxacin pharmacokinetics are linear and predictable after single and multiple oral dosing regimens. Steady-state conditions are reached within 48 hours following a 500 mg or 750 mg once-daily dosage regimen. The peak and trough plasma concentrations attained following multiple once-daily oral dosage regimens were approximately 5.7 mcg/mL and 0.5 mcg/mL after the 500 mg doses, and 8.6 mcg/mL and 1.1 mcg/mL after the 750 mg doses, respectively.

There was no clinically significant effect of food on the extent of absorption of levofloxacin. Oral administration with food slightly prolongs the time to peak concentration by approximately 1 hour, and slightly decreases the peak concentration by approximately 14%. Therefore, levofloxacin can be administered without regard to food.

Distribution:
The mean volume of distribution of levofloxacin generally ranges from 74 to 112 L after single and multiple 500 mg or 750 mg doses, indicating widespread distribution into body tissues. Levofloxacin reaches its peak levels in skin tissues (11.7 mcg/g for a 750 mg dose) and in blister fluid (4.33 mcg/g for a 500 mg dose) at approximately 3-4 hours after dosing. The skin tissue biopsy to plasma AUC ratio is approximately 2. The blister fluid to plasma AUC ratio is approximately 1, following multiple once-daily oral administration of 750 mg and 500 mg levofloxacin to healthy subjects, respectively. Levofloxacin also penetrates into lung tissues.
Lung tissue concentrations were generally 2- to 5-fold higher than plasma concentrations, and ranged from approximately 2.4 to 11.3 mcg/g over a 24-hour period after a single 500 mg oral dose.

Levofloxacin is 24 to 38% bound to serum proteins across all species studied. Levofloxacin binding to serum proteins is independent of the drug concentration.

Metabolism:
Levofloxacin is stereochemically stable in plasma and urine, and does not invert metabolically to its enantiomer, D-ofloxacin. Levofloxacin undergoes limited metabolism in humans, and is primarily excreted as unchanged drug (87%) in the urine within 48 hours.

Excretion:
The major route of elimination of levofloxacin in humans is as unchanged drug in the urine. The mean terminal plasma elimination half-life of levofloxacin ranges from approximately 6 to 8 hours following single or multiple doses of levofloxacin given orally.

Special Populations and Conditions

Pediatrics: The pharmacokinetics of levofloxacin in pediatric patients have not been studied.

Geriatrics: There are no significant differences in levofloxacin pharmacokinetics between young and elderly subjects when the subjects' differences in creatinine clearance are taken into consideration. Drug absorption appears to be unaffected by age. Levofloxacin dose adjustment based on age alone is not necessary.

Gender: There are no significant differences in levofloxacin pharmacokinetics between male and female subjects when the differences in creatinine clearance are taken into consideration. Dose adjustment based on gender alone is not necessary.

Race: The apparent total body clearance and apparent volume of distribution were not affected by race in a covariate analysis performed on data from 72 subjects.

Hepatic Insufficiency: Pharmacokinetic studies in hepatically impaired patients have not been conducted. Due to the limited extent of levofloxacin metabolism, the pharmacokinetics of levofloxacin are not expected to be affected by hepatic impairment.

Renal Insufficiency: Pharmacokinetic parameters of levofloxacin following oral or intravenous doses of levofloxacin in patients with impaired renal function (creatinine clearance ≤ 80 mL/min) are presented in Table 1.5. Clearance of levofloxacin is reduced and plasma elimination half-life is prolonged in this patient population. Dosage adjustment may be required in such patients to avoid accumulation.

A dosage reduction is being recommended depending on the levels of renal insufficiency. Dosing recommendations are based on pharmacokinetic modelling of data collected from a clinical safety and pharmacokinetic study in renally impaired patients treated with a single 500 mg oral dose of levofloxacin.

Neither hemodialysis nor continuous ambulatory peritoneal dialysis (CAPD) is effective in removal of levofloxacin from the body, indicating supplemental doses of levofloxacin are not required following hemodialysis or CAPD.

Bacterial Infection: The pharmacokinetics of levofloxacin in patients with community-acquired bacterial infections are comparable to those observed in healthy subjects.

MICROBIOLOGY

Levofloxacin is the L-isomer of the racemate, ofloxacin, a quinolone antibacterial agent. The antibacterial activity of ofloxacin resides primarily in the L-isomer. The mechanism of action of levofloxacin and other quinolone antibacterials involves inhibition of bacterial topoisomerase II (DNA gyrase) and topoisomerase IV, enzymes required for DNA replication, transcription, repair, and recombination. In this regard, the L-isomer produces more hydrogen bonds and therefore, more stable complexes with DNA gyrase than does the D-isomer. Microbiologically, this translates into a 25- to 40-fold greater antibacterial activity for the L-isomer, levofloxacin, over the D-isomer. Quinolones rapidly and specifically inhibit bacterial DNA synthesis.

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Levofloxacin has *in vitro* activity against a broad spectrum of gram-positive and gram-negative aerobic and anaerobic bacteria. Levofloxacin is often bactericidal at concentrations equal to or greater than the Minimum Inhibitory Concentrations (MIC). The *in vitro* activity of levofloxacin against clinical isolates is summarized in Table 2.48.

Table 2.48 - *In Vitro* Activity of Levofloxacin against Clinical Isolates

Organism	(# of	MIC (mcg/mL)		
		50%	90%	Range
Acinetobacter baumannii	(57)	0.120	16.000	0.060->16.000
Acinetobacter calcoaceticus	(48)	0.250	0.250	0.030-64.000
Chlamydia pneumoniae	(10)	0.250	0.250	0.125-0.500
Citrobacter diversus	(20)	0.030	0.030	0.015-0.060
Citrobacter freundii	(50)	0.060	1.000	0.015-8.000
Enterobacter spp.	(200)	0.060	0.500	≤0.008->16.000
Enterobacter aerogenes	(44)	0.250	0.500	0.060-2.000
Enterobacter agglomerans	(13)	0.250	0.250	0.060-0.500
Enterobacter cloacae	(97)	0.250	0.500	0.025-16.000
Enterococcus spp.	(162)	1.000	>16.00	0.500->16.000
Enterococcus (Streptococcus) faecalis	(122)	1.000	16.000	0.250-64.000
Escherichia coli	(817)	0.030	0.060	≤0.008->16.000
Haemophilus influenzae	(94)	0.015	0.015	≤0.008-0.030
Haemophilus parainfluenzae	(127)	0.250	0.250	0.015-1.000
Haemophilus parahemolyticus	(12)	0.250	0.250	0.008-0.250
Klebsiella spp.	(345)	0.060	1.000	0.015-16.000
Klebsiella oxytoca	(43)	0.250	0.250	0.030-2.000
Klebsiella pneumoniae	(225)	0.250	0.500	0.060-18.000
Legionella pneumophila	(10)		0.030	0.0079-0.030
Moraxella (Branhamella) catarrhalis	(110)	0.250	0.250	0.0150-1.000
Morganella morganii	(43)	0.060	1.000	0.0150->16.000
Mycoplasma pneumoniae	(60)	0.250	0.500	0.250-0.500
Neisseria gonorrhoeae	(47)	≤ 0.008	0.016	≤0.008-0.060
Neisseria meningitidis	(13)	0.250	0.250	0.250-0.500
Proteus and *Providencia spp.*	(36)	0.060	1.000	0.015->16.000
Proteus mirabilis	(123)	0.060	0.120	0.015-4.000
Proteus vulgaris	(14)	0.250	0.250	0.250-0.500
*Pseudomonas aeruginosa**	(378)	1.000	8.000	0.030->16.000
Pseudomonas maltophilia	(17)	0.500	2.000	0.250-4.000
Salmonella spp.	(10)	0.060	0.060	0.060-0.250
Serratia spp.	(65)	0.120	0.500	0.030->16.000
Serratia marcescens	(42)	0.250	1.000	0.125-4.000
Staphylococcus aureus	(565)	0.250	0.500	0.125-32.000

Organism	(# of isolates	MIC cg/mL)		
		50%	90%	Range
Staphylococcus aureus, methicillin- resistant	(25)	0.250	0.500	0.120-1.000

Staphylococcus aureus, methicillin- susceptible	(25)	0.250	0.500	0.120-0.500
Staphylococcus aureus, oxacillin-resistant	(62)	8.000	>16.00	0.120->16.000
Staphylococcus aureus, oxacillin-susceptible	(367)	0.120	0.500	0.030-16.000
Staphylococcus epidermidis	(47)	0.250	8.000	0.250-32.000
Staphylococcus epidermidis, methicillin- resistant (MRSE)	(14)	0.250	0.250	0.120-0.500
Staphylococcus epidermidis, methicillin- susceptible (MSSE)	(12)	0.250	1.000	0.250-1.000
Staphylococcus saprophyticus	(16)	0.500	1.000	0.250-2.000
Stenotrophomonas maltophilia	(43)	2.000	16.000	0.250-16.000
Streptococcus (Viridans group)	(8)	0.750	1.000	0.250-1.000
Streptococcus (Group C)	(28)	0.500	1.000	0.250-2.000
Streptococcus (Group G)	(34)	0.500	1.000	0.250-2.000
Streptococcus agalactiae	(96)	1.000	2.000	0.500-2.000
Streptococcus milleri	(35)	0.500	1.000	0.250-4.000
Streptococcus pneumoniae	(99)	1.000	1.000	0.500-2.000
Streptococcus pneumoniae, penicillin- susceptible (MIC ≤0.06	(2699)	0.500	1.000	≤0.004->8.000
Streptococcus pneumoniae, penicillin-resistant (MIC ≥2.0 mcg/mL)†	(538)	0.500	1.000	≤0.004-2.000
Streptococcus pneumoniae, clarithromycin- susceptible (MIC≤0.25	(502)	0.500	1.000	0.250->16.000
Streptococcus pneumoniae, clarithromycin- resistant (MIC ≥1.0	(136)	1.000	2.000	0.12-16.000
Streptococcus pneumoniae, erythromycin- resistant (MIC ≥1.0	(27)	1.000	1.000	0.500-16.000
Streptococcus pyogenes	(87)	0.500	1.000	0.250-2.000
Streptococcus sanguis	(19)	1.000	2.000	0.250-2.000

* As with other drugs in this class, some strains of *Pseudomonas aeruginosa* may develop resistance fairly rapidly during treatment with levofloxacin.

*Data obtained for isolates from Complicated Skin and Skin Structure clinical studies, and literature, indicate the MIC value has increased for MRSA Based on NCCLS classification

Levofloxacin is not active against *Treponema pallidum*

Resistance

Resistance to levofloxacin due to spontaneous mutation *in vitro* is a rare occurrence (range: 10^{-8} to 10^{-10}). Although cross-resistance has been observed between levofloxacin and other fluoroquinolones, some organisms resistant to other quinolones, including ofloxacin, may be susceptible to levofloxacin.

Susceptibility Tests

Susceptibility testing for levofloxacin should be performed, as it is the optimal predictor of activity.

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STORAGE AND STABILITY

LEE-FLOX Tablets should be stored at a temperature not exceeding 30ºC, in dry place.

Shelf life: 3 Years

Packaging

- Lee-flox 250 mg tablets: carton box containing one (Al/ transparent colorless PVC) strip of five film coated tablets + insert leaflet.
- Lee-flox 500 mg tablets: carton box containing one (Al/ transparent colorless PVC) strip of 5 film coated tablets + insert leaflet.
- Lee-flox 500 mg tablets: carton box containing 100 (Al/ transparent colorless PVC) strips each of 5 film coated tablets + insert leaflet. (For Tenders only)
- Lee-flox 750 mg tablets: carton box containing one (Al/ White opaque PVC) strip of 7 film coated tablets + insert leaflet.
- Lee-flox 750 mg tablets: carton box containing 100 (Al/ White opaque PVC) strips each of 7 film coated tablets + insert leaflet. (For Tenders only)

Manufacturer & License holder:

Pharaonia Pharmaceuticals (Pharo Pharma)
New Borg El Arab city – 3rd Industrial zone – block no. 16 – Part (1) – Alexandria – Egypt.

لي-فلوكس250 مجم 500 مجم & 750 مجم
ليفوفلوكساسين
اقراص مغلفة

اقرأ بعناية قبل البدء في تناول لي-فلوكس وفي كل مرة تحصل على علبة جديدة.
هذه النشرة هي ملخص ولن تخبرك بكل شيء عن هذا الدواء. تحدث إلى أخصائي الرعاية الصحية الخاص بك حول حالتك الطبية وعلاجك واسأل عما إذا كان هناك أي معلومات جديدة عن لي-فلوكس.

تحذيرات واحتياطات خطيرة

تحدث إلى طبيبك إذا كنت:
-لديك رد فعل تحسسي خطير لليفوفلوكساسين أو مضادات حيوية مماثلة مثل سيبروفلوكساسين ، موكسيفلوكساسين ، وغيرها.
- لديك نوبات (تشنجات). أخبر طبيبك إذا كان لديك أي مشاكل في الدماغ ، بما في ذلك الصرع. سيخبرك طبيبك ما إذا كان يجب عليك استخدام هذا الدواء.
- لديك مشاكل عضلية (مثل ضعف ، مشاكل في المفاصل). لا تستخدم لي-فلوكس إذا كنت تعاني أو كنت تعاني من الوهن العضلي الشديد.
- لديك تاريخ سابق لالتهاب الأوتار (الألياف التي تربط العظام بالعضلات في الجسم) وتمزق الأوتار. يكون خطر إصابتك بمشكلة الأوتار أكبر ، إذا كان عمرك يزيد عن 60 عامًا ، وإذا كنت تتناول أدوية الستيرويد ، أو إذا كنت قد أجريت عملية زرع كلية أو قلب أو رئة.
-لديك تاريخ عائلي للإصابة بمتلازمة QT الطويلة (إطالة ضربات القلب في اختبار مخطط كهربية القلب).

ما هو استخدام لي-فلوكس ؟
يستخدم لي-فلوكس لعلاج الالتهابات البكتيرية في:
- الجلد.
- الكلى.
- المسالك البولية (المثانة أو البروستاتا).
- الجيوب.
- الرئتين.

كيف يعمل لي-فلوكس ؟
يوجد لي-فلوكس في مجموعة من المضادات الحيوية تسمى كينولونز التي:
- يوقف نمو البكتيريا.
- اقتل البكتيريا.
- التقليل من الإصابة.
تحدث بعض أنواع العدوى بسبب الفيروسات ، مثل نزلات البرد. لي-فلوكس لا يقتل الفيروسات.

لا تستخدم لي-فلوكس:
- لديك رد فعل تحسسي لهذا الدواء أو لمضادات حيوية أخرى من الكينولون (مثل سيبروفلوكساسين ، موكسيفلوكساسين).
- لديك تاريخ سابق لالتهاب الأوتار (إلتهاب في الأوتار أو تمزق الأوتار) أثناء العلاج بمضاد حيوي اخر ينتمي إلي عائلة كينولون.
تسبب هذه الحالة الألم والحنان خارج المفصل مباشرة في الكتفين والمرفقين والمعصمين والركبتين والكعب وما إلى ذلك.
للمساعدة في تجنب الآثار الجانبية وضمان الاستخدام السليم ، تحدث إلى أخصائي الرعاية الصحية الخاص بك قبل تناول لي-فلوكس.
تحدث عن أي حالات أو مشاكل صحية قد تكون لديك ، بما في ذلك إذا كنت:
- لديك مشاكل في الكلى.
- مصاب بالصرع.
- كان لديك أو كان لديك نوبات (تشنجات).
- عانيت من أي مشاكل في نظم قلبك أو معدل ضربات قلبك أو مشاكل في نقص البوتاسيوم.

Dr/Shaza 25/3/2024

- مصاب بمرض السكري ويتناولون أدوية مضادة للسكر (قد يؤثر ذلك على مستويات السكر في الدم).
- كنت تعانين من مرض يسبب ضعف العضلات (الوهن العضلي الوبيل).
- تعاني من أي أعراض لضعف العضلات ، بما في ذلك صعوبات في التنفس (مثل ضيق التنفس).
- لديك تاريخ من مشاكل الأوتار المرتبطة بالمضادات الحيوية.
- حامل أو تخططين للحمل.
- كنت ترضعين أو تخططين للإرضاع. تحدث إلى طبيبك حول كيفية إطعام طفلك أثناء تناول لي-فلوكس.
- لديك تمدد الأوعية الدموية الأبهري وهو انتفاخ غير طبيعي في وعاء دموي كبير يسمى الشريان الأورطي.
- لديك أو إذا كان أي فرد في عائلتك يعاني من حالة تسمى مرض تمدد الأوعية الدموية وهو انتفاخ غير طبيعي في أي وعاء دموي كبير في الجسم.
- لديك تسلخ الأبهر وهو تمزق في جدار الشريان الأورطي.
- لديك أي من الحالات التالية: متلازمة مارفان ، متلازمة إيلرز دانلوس الوعائية ، متلازمة تيرنر أو متلازمة سجوجرن (التهاب أمراض المناعة الذاتية)، التهاب الشرايين تاكاياسو ، التهاب الشرايين ذو الخلايا العملاقة أو مرض بهجت.
- لديك ارتفاع في ضغط الدم
- لديك تصلب الشرايين ، وهو تصلب الأوعية الدموية والتهاب المفاصل الروماتويدي (مرض المفاصل) أو التهاب الغشاء المبطن للقلب..

ما هي أهم المعلومات التي يجب أن أعرفها؟
- تفاقم الوهن العضلي الشديد (مرض يسبب ضعف العضلات). قد تسبب الفلوروكينولونات تفاقم أعراض الوهن العضلي الشديد ، بما في ذلك ضعف العضلات ومشاكل التنفس.
اتصل بمقدم الرعاية الصحية الخاص بك على الفور إذا كان لديك أي تدهور
ضعف العضلات أو مشاكل في التنفس.
أخبر مقدم الرعاية الصحية الخاص بك عن جميع حالاتك الطبية ، بما في ذلك إذا كان لديك مرض يسبب ضعف العضلات (الوهن العضلي الوبيل).

تحذيرات أخرى يجب أن تعرفها عن:
تغيرات سكر الدم
الأدوية مثل لي-فلوكس يمكن أن تسبب ارتفاع وانخفاض مستويات السكر في الدم لدى مرضى السكري. شوهدت حالات خطيرة من نقص السكر في الدم (انخفاض مستويات السكر في الدم) التي تسببت في غيبوبة أو الوفاة باستخدام أدوية مثل لي-فلوكس. إذا كنت مصابًا بداء السكري ، فافحص مستويات السكر في الدم كثيرًا أثناء تناول لي-فلوكس.
إذا كنت مصابًا بداء السكري ، فقد تصاب بتفاعل سكر الدم (انخفاض سكر الدم) مع أعراض شائعة مثل:
-دوخة.
- الجوع المفرط.
- قلة التنسيق.
-صداع الرأس.
-إعياء.
-إغماء.
أو تفاعل فرط سكر الدم (ارتفاع سكر الدم) مع أعراض شائعة مثل:
-العطش الشديد.
- كثرة التبول.

ارتبطت الكينولونات ، بما في ذلك الليفوفلوكساسين ، بتضخم أو "انتفاخ" وعاء دموي كبير (تمدد الأوعية الدموية الأبهري أو تمدد الأوعية الدموية المحيطية للأوعية الكبيرة) وتسلخ الأبهر (تمزق في جدار الشريان الأبهر)
يكون خطر حدوث هذه المشكلات أعلى إذا:
- كبار السن

- لديك أو أي شخص في عائلتك مصاب بمرض تمدد الأوعية الدموية
- لديك تمدد الأوعية الدموية الأبهري أو تسلخ الأبهر
- لديك أي من الحالات التالية: متلازمة مارفان ، متلازمة إيلرز دانلوس الوعائية ، التهاب الشرايين تاكاياسو أو التهاب الشرايين ذو الخلايا العملاقة أو مرض بهجت.
- لديك إرتفاع في ضغط الدم أو تصلب الشرايين

إذا شعرت بألم حاد ومفاجئ في بطنك أو صدرك أو ظهرك ، أو إحساس بالنبض في بطنك ، أو دوار أو فقدان للوعي ، فعليك الحصول على مساعدة طبية فورية. قد تزداد مخاطرك إذا كنت تعالج بالكورتيكوستيرويدات الجهازية.
اذا بدأت تعاني من بداية سريعة لضيق التنفس ، خاصة عند الاستلقاء على سريرك ، أو لاحظت تورّم في الكاحلين أو القدمين أو البطن ، أو احساس بخفقان القلب (الإحساس بنبض قلب سريع أو غير منتظم) يجب إبلاغ الطبيب على الفور.

ما هي الآثار الجانبية المحتملة (من استخدام لي-فلوكس)؟
الآثار الجانبية ذاتية الحد
- الشعور بالدوار
- الأرق (صعوبة النوم).
-كوابيس
يجب عليك الاتصال بطبيبك إذا واجهت أيًا من هذه الأعراض.

رد فعل تحسسي:
إذا شعرت بواحد مما يلي:
-قشعريرة.
-مثير للحكة.
-الطفح الجلدي.
- صعوبة التنفس أو البلع.
- تورم في الوجه أو اللسان أو الحلق.
- أعراض أخرى لرد فعل تحسسي.
يجب عليك التوقف عن تناول هذا الدواء والاتصال بطبيبك.

تشغيل الآلات الثقيلة:
يجب أن تعلم أن استخدام لي-فلوكس قد يسبب الدوار. يرجى التأكد من أنك تعرف كيفية التصرف إذا كنت:
- تقود سيارة.
- تشغل أي آلة في مكان العمل.
- أداء العمل الذي يحتاج اليقظة الذهنية أو التنسيق.

التعرض لأشعة الشمس:
يجب ألا تعرض نفسك لأشعة الشمس أو الأشعة فوق البنفسجية الاصطناعية أثناء تناولك لـ لي-فلوكس. استخدم واقي الشمس وارتد ملابس واقية إذا كنت بالخارج في الشمس

أخبر أخصائي الرعاية الصحية الخاص بك عن جميع الأدوية التي تتناولها ، بما في ذلك أي أدوية أو فيتامينات أو معادن أو مكملات طبيعية أو أدوية بديلة.
قد يتفاعل ما يلي مع لي-فلوكس:
- مضادات الحموضة ، فيتامينات متعددة ، أو منتجات تحتوي على معادن (مثل الألمنيوم ، الكالسيوم ، الحديد ، الماغنسيوم أو الزنك). انظر كيف تتناول لي-فلوكس .
- الأدوية المستخدمة للقرحة (مثل سوكرالفات). انظر كيف تتناول لي-فلوكس.

- الأدوية المستخدمة لحرقة المعدة أو النقرس (مثل البروبينسيد ، سيميتيدين ، إلخ).
- الأدوية المستخدمة لعلاج الربو أو مرض الانسداد الرئوي المزمن (مثل الثيوفيلين).
- أدوية لالتهاب المفاصل (مضادات الالتهاب غير الستيرويدية (المسكنات) مثل ايبوبروفين ، نابروكسين).
- أدوية السكر في الدم (مثل ميتفورمين ، جليكلازيد ، أنسولين ، إلخ).
- الأدوية المستعملة لأية أمراض قلبية.
- أدوية منع تجلط الدم (مثل الوارفارين ، إلخ) التي تستخدم لتسييل الدم ومنع تجلط الدم - قد تعرضك لمشاكل النزيف.

قد يتداخل هذا الدواء مع بعض الاختبارات المعملية (مثل فحص البول بحثًا عن المواد الأفيونية) ، مما قد يتسبب في نتائج اختبار خاطئة.

كيف تتناول لي-فلوكس:
يجب أن تبتلع القرص كاملاً (دون تقسيم)مع الطعام أو بدونه.

حاول تناول الأقراص في نفس الوقت وشرب الكثير من السوائل أثناء تناول هذا الدواء ما لم يوجه طبيبك غير ذلك.
لا تشارك دوائك مع أي شخص.

الأدوية المضادة للبكتيريا مثل لي-فلوكس تعالج الالتهابات البكتيرية فقط. انهم لا يعالجون الالتهابات الفيروسية. على الرغم من أنك قد تشعر بتحسن في وقت مبكر من العلاج ، يجب استخدام لي-فلوكس تمامًا وفقًا للتوجيهات. يمكن أن يؤدي سوء استخدام لي-فلوكس أو الإفراط في استخدامه إلى نمو البكتيريا التي لن تقتلها لي-فلوكس (المقاومة). هذا يعني أن لي-فلوكس قد لا يعمل في المستقبل.

اسأل الصيدلي عن المنتجات الأخرى التي تتناولها. ستؤثر بعض الأدوية على طريقة امتصاص جسمك لـ لي-فلوكس. تناول لي-فلوكس قبل ساعتين على الأقل أو بعد ساعتين من تناول هذه الأدوية. تتضمن بعض الأمثلة: الفيتامينات / المعادن (بما في ذلك مكملات الحديد والزنك) والمنتجات التي تحتوي على المغنيسيوم أو الألومنيوم أو الكالسيوم (مثل مضادات الحموضة ومكملات الكالسيوم).

جرعة الكبار المعتادة:
يجب أن تتناول هذا الدواء عن طريق الفم حسب توجيهات الطبيب.
تعتمد الجرعة وطول مدة العلاج على وظيفة الكلى والحالة الطبية والاستجابة للعلاج. قد يستمر لمدة 3 أو 5 أو 7 أو 10 أو 14 أو 28 يومًا حسب حالتك.
أخبر طبيبك إذا لم تتحسن حالتك.

جرعة مفرطة:
قد تشمل أعراض الجرعة الزائدة: دوار شديد.

الجرعة الفائتة:
إذا فاتتك جرعة ، تناولها حالما تتذكرها. إذا كان قريبًا من وقت الجرعة التالية ، فتجاوز الجرعة الفائتة واستأنف جدول الجرعات المعتاد.
لا تضاعف الجرعة للحاق بها.

ما هي الآثار الجانبية المحتملة لاستخدام لي-فلوكس ؟
هذه ليست كل الآثار الجانبية المحتملة التي قد تشعر بها عند تناول لي-فلوكس. إذا واجهت أي آثار جانبية غير مدرجة هنا ، فاتصل بأخصائي الرعاية الصحية الخاص بك.

الآثار الجانبية الخطيرة وماذا تفعل حيالها
تحدث إلى أخصائي الرعاية الصحية الخاص بك في حالة الاعراض الاتيه :
شائع جدا
- غثيان
- صداع الراس
- الإسهال (يكون البراز ليّنًا إلى مائي)

- الأرق (قلة النوم)
- الدوخة (النعاس ، خفة الرأس)
- الإمساك (صعوبة إخراج البراز)

شائع

- آلام في البطن أو المعدة أو عدم الراحة
- التقيؤ
- عسر الهضم (عدم الراحة أو الألم في الجزء العلوي من البطن)
- ضيق التنفس (ضيق التنفس)
- داء المونيلاز (عدوى الخميرة في الفم والحلق)
- الطفح الجلدي
- حكة (حكة)
- حكة وإفرازات في المهبل
- الاستسقاء (التورم الناجم عن السوائل الزائدة في جسمك)
- ألم في الصدر

نادر

- **تقلصات أو ألم في المعدة (شديد)**
- **هلوسة أو الشعور بجنون العظمة**
- **الشعور بالهياج**
- **تشنجات**
- **الشعور بلسعة)وخز(و /أو تنميل**
- **ضعف بالعضلات**
- بثور
- ارتباك
- الإسهال (المائي والشديد) الذي قد يكون دمويًا أيضًا
- الشعور بأن الآخرين يمكنهم سماع أفكارك أو التحكم في سلوكك
- حُمى
- **ألم أو التهاب أو تورم في الساقين أو الكتفين أو اليدين ، بما في ذلك تمزق الأوتار أو تورم الأوتار (التهاب الأوتار)**
- **احمرار وتورم الجلد**
- رؤية أو سماع أو الشعور بأشياء غير موجودة
- إحساس بالحرقان على الجلد
- **مزاج حاد أو تغيرات عقلية والتى يمكن أن تؤدى فى حالات نادرة الى إلي ايذاء نفسك**
- **الاعتلال العصبي (مشاكل في الأعصاب مثل الألم والحرق والوخز والخدر أو الضعف)**
- طفح جلدي أو حكة أو احمرار - حساسية من أشعة الشمس (حساسية للضوء) ، والتي يمكن أن تظهر على شكل اندفاع جلدي أو شديد
- ارتجاف
- سلوك غير عادي

امراض عقليه:

- القلق
- ارتباك
- اكتئاب

- الشعور بالاضطراب
- قلق أو عصبي
- أفكار أو أفعال انتحارية
- هلوسة
- عدم القدرة على التفكير بوضوح أو الانتباه
- فقدان الذاكرة
- جنون العظمة أو فقدان الاتصال بالواقع

مشاكل عصبية:

- نوبات (تشنجات).
- رعاش
  ارتفاع الضغط داخل جمجمتك.
- عدم وضوح الرؤية أو ازدواجها
- الصداع
- غثيان
  نقص السكر في الدم (انخفاض سكر الدم):
- تغير في المزاج

- دوخة
- سرعة ضربات القلب
- الشعور بالإغماء
- صداع
- الجوع
- تهتز
- التعرق
- ضعف

توقف عن تناول الدواء واحصل على مساعدة طبية فورية في حالة:

- صداع شديد / مستمر
- إذا كنت تعاني من الم ، تصلب أو تورم في المفاصل
- تغيرات الرؤية
- الاهتزازات ، النوبات (التشنجات)
- دوار شديد ، إغماء
- ضربات قلب سريعة / غير منتظمة
- علامات مشاكل الكبد (مثل الغثيان / القيء المستمر ، آلام في المعدة / البطن ، إرهاق غير عادي ، اصفرار العينين / الجلد ، البول الداكن)

- **تمدد الأوعية الدموية الأبهري (انتفاخ غير طبيعي في وعاء دموي كبير يسمى الشريان الأورطي) / تسلخ الأبهر (تمزق في جدار الشريان الأورطي):** دوار ، فقدان الوعي ، إحساس بالنبض في البطن ، ألم مفاجئ وشديد في البطن أو الصدر أو الظهر.

إذا كان لديك عرض مزعج أو عرض جانبي غير مذكور هنا أو أصبح سيئًا بما يكفي للتدخل في أنشطتك اليومية ، فتحدث إلى أخصائي الرعاية الصحية الخاص بك.

الإبلاغ عن الآثار الجانبية
عند حدوث أي آثار جانبية، فتحدث إلى مقدم الرعاية الصحية. وهذا يشمل الآثار الجانبية الغير مدرجة في هذه النشرة.
خدمة أثر جانبي على الموقع الإلكتروني لهيئة الدواء المصرية https://www.edaegypt.gov.eg/ar/
عبر البريد الإلكتروني: Pv.followup@edaegypt.gov.eg
الاتصال بالخط الساخن: 15301
فمن خلال الإبلاغ عن الآثار الجانبية، يمكنك المساعدة في تقديم المزيد من المعلومات عن سلامة هذا الدواء

التخزين والعبوة ومعلومات اخري
يحفظ في درجة حرارة لاتتعدى 30 درجة مئوية في مكان جاف

مدة الصلاحية: 3 سنوات

المكونات :
المادة الفعالة:
لي-فلوكس 750:
ليڤوفلوكساسين هيدروكلوريد 825.75 مجم يكافئ ليڤوفلوكساسين 750 مجم
لي-فلوكس 500:
ليڤوفلوكساسين هيدروكلوريد 550.5 مجم يكافئ ليڤوفلوكساسين 500 مجم
لي-فلوكس 250:
ليڤوفلوكساسين هيدروكلوريد 275.25 مجم يكافئ ليڤوفلوكساسين 250 مجم
المواد غير الفعالة:
لي- فلوكس250 :
لاكتوز احادي المائية، كروسكارميللوز صوديوم ، بوڤيدون K30 ،ماغنسيوم ستيرايت ، هيدروكسي بروبيل ميثيل سيليولوز ، تيتانيوم داى أوكسيد ، بودرة تلك ، بولى إيثيلين جيليكول 6000،
لي- فلوكس 500:
لاكتوز احادي المائية، كروسكارميللوز صوديوم ، بوڤيدون K30 ،ماغنسيوم ستيرايت ، هيدروكسي بروبيل ميثيل سيليولوز ، تيتانيوم داى أوكسيد ، بودرة تلك ، بولى إيثيلين جيليكول 6000
لي- فلوكس 750:
لاكتوز، كروسكارميللوز صوديوم ، بوڤيدون K30 ،ماغنسيوم ستيرايت ، ميثوثيل، تيتانيوم داى أوكسيد ، بودرة تلك ، بولى إيثيلين جيليكول6000، لون D&C أحمر رقم30 ،أوكسيد الحديد الأحمر

العبوة:
لي- فلوكس250:- علبة كرتون تحتوى على 5 أقراص فى شريط (الومنيوم /بي في سي شفاف عديم اللون) ومعها نشرة.
لي- فلوكس500:- علبة كرتون تحتوى على 5 أقراص فى شريط (الومنيوم /بي في سي شفاف عديم اللون)
لي-فلوكس 500:- علبة كرتون تحتوى على 100شريط (الومينوم/ PVC بي في سي شفاف) كل شريط يحتوى على 5 أقراص ومعها نشرة (للمناقصات فقط)
لي- فلوكس750:- علبة كرتون تحتوى على 7 أقراص فى شريط (الومنيوم /بي في سي ابيض معتم)ومعها نشرة.
لي-فلوكس 750:- علبة كرتون تحتوى على 100شريط (الومينيوم / بي في سي شفاف ابيض معتم) كل شريط يحتوى على 7 أقراص

ومعها نشرة (للمناقصات فقط)

الخصائص الفيزيائية:
لي-فلوكس 250 مجم: قرص ابيض الي ابيض داكن مغلف دائري الشكل و محدب الوجهين
لي-فلوكس500 مجم: قرص ابيض ابيض داكن مغلف دائري الشكل و محدب الوجهين

لي فلوكس 750 مجم: قرص وردي مغلف بيضاوي الشكل و محدب الوجهين

صاحب الرخصة التسويقية و المنتج:
الشركة الفرعونية للأدوية (فارو فارما)
مدينة برج العرب الجديدة - المنطقة الصناعية الثالثة - بلوك 16 - قطعة رقم (1) ج.م.ع.