Levoget™

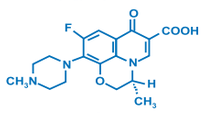
[Levofloxacin USP]

500mg/100mL
750mg/150mL
I.V. Infusion

DESCRIPTION

Levoget (Levofloxacin) is a synthetic broad-spectrum antibacterial agent. Chemically, levofloxacin, a chiral fluorinated carboxyquinolone, is the pure (-) (S)-enantiomer of the racemic drug substance ofloxacin with a chemical name of: (-)-(S)-9-fluoro-2, 3-dihydro-3-methyl-10- (4-methyl-piperazinyl)-7-oxo-7H pyrido [1,2,3,-de] [1,4] benzoxazine-6-carboxylic acid.

The molecular formula is $C_{18}H_{20}FN_3O_4$ and the structural formula is:



Levofloxacin

QUALITATIVE AND QUANTITATIVE COMPOSITION

Levoget (Levofloxacin) Infusion is available as:

1. Levoget I.V Infusion 500mg/100mL
   Each mL of solution for infusion contains:
   Levofloxacin USP...5mg

2. Levoget I.V Infusion 750mg/150mL
   Each mL of solution for infusion contains:
   Levofloxacin USP...5mg

CLINICAL PHARMACOLOGY

Mechanism of Action

Levofloxacin is the L-isomer of the racemate, ofloxacin, a quinolone antimicrobial agent. The antibacterial activity of ofloxacin resides primarily in the L-isomer. The main mechanism of action of levofloxacin involves the inhibition of bacterial topoisomerase IV and DNA gyrase (both or which are type II topoisomearse), enzymes required for DNA replication, transcription, repair and recombination.

Levofloxacin has *in-vitro* activity against the following gram-negative and gram positive micro-organisms. It is often bactericidal at concentrations equal to or slightly greater than inhibitory concentration.It is generally considered to be about twice as active as its isomer, ofloxacin.

Microbiology

Levofloxacin has been shown to be active against most strains of the following micro-organisms.

Commonly susceptible species:

Aerobic Gram-positive bacteria
Bacillus anthracis
Staphylococcus aureus methicillin-susceptible
Staphylococcus saprophyticus
Streptococci, group C and G
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes

Aerobic Gram- negative bacteria
Eikenella corrodens
Haemophilus influenzae
Haemophilus para-influenzae
Klebsiella oxytoca
Moraxella catarrhalis
Pasteurella multocida
Proteus vulgaris
Providencia rettgeri

Anaerobic bacteria
Peptostreptococcus

Other
Chlamydophila pneumoniae
Chlamydophila psittaci
Chlamydia trachomatis
Legionella pneumophila
Mycoplasma pneumoniae
Mycoplasma hominis
Ureaplasma urealyticum

Species for which acquired resistance may be a problem

Aerobic Gram-positive bacteria
Enterococcus faecalis
Staphylococcus aureus methicillin-resistant#
Coagulase negative Staphylococcus spp

Aerobic Gram- negative bacteria
Acinetobacter baumannii
Citrobacter freundii
Enterobacter aerogenes
Enterobacter cloacae
Escherichia coli
Klebsiella pneumoniae
Morganella morganii
Proteus mirabilis
Providencia stuartii
Pseudomonas aeruginosa
Serratia marcescens

Anaerobic bacteria
Bacteroides fragilis

Inherently resistant Strains
Aerobic Gram-positive bacteria
Enterococcus faecium
#Methicillin-resistant S. aureus are very likely to possess co-resistance to fluoroquinolones, including levofloxacin.

Pharmacokinetics

Absorption

Following a single intravenous dose of levofloxacin, the mean ±SD peak plasma concentration attained was 6.2 ±1.0µg/mL after a 500mg dose infused over 60 minutes and 11.5 ±4.0µg/mL after a 750mg dose infused over 90 minutes.

Levofloxacin IV pharmacokinetics are linear and predictable after single and multiple dosing regimens. Steady state conditions are reached within 48 hours following a 500mg or 750mg once daily dosage regimens. The mean ±SD peak and trough plasma concentrations attained following multiple once-daily I.V. regimens were approximately 6.4 ±0.8 and 0.6 ±0.2µg/mL after the 500mg doses 12,1 ± 4,1 and 1,3 ±0,71µg/mL after the 750mg doses, respectively.

Distribution

The mean volume of distribution generally ranges from 74 – 112 litres after single and multiple dosing of 500mg or 750mg dose, indicating widespread distribution into body tissues. Levofloxacin reaches its peak levels in skin tissues and in body fluid of healthy subjects at approximately 3 hours after dosing.

Levofloxacin is approximately 24 to 38% bound to serum proteins. Levofloxacin is mainly bound to serum albumin in humans. The binding of levofloxacin to serum proteins is independent of the drug concentration.

Metabolism and Elimination

Levofloxacin undergoes limited metabolism in humans and is primarily excreted as unchanged drug in the urine. Less than 5% of an administered dose was recovered in the urine as the desmethyl and N-oxide metabolites, the only metabolites identified in humans. The mean terminal elimination half-life ($t_{1/2}$) of levofloxacin ranges from approximately 6 to 8 hours following single or multiple doses of levofloxacin. The mean apparent total body clearance and renal clearance range from approx. 144-226mL/min and 96-142mL/min respectively.

Special Populations

Subjects with renal insufficiency

The pharmacokinetics of levofloxacin are affected by renal impairment. With decreasing renal function renal elimination and clearance are decreased, and elimination half-lives increased as shown in the table below:

Pharmacokinetics in renal insufficiency following single oral 500 mg dose

Clcr [ml/min]	< 20	20 - 40	50 - 80
Cl_R [ml/min]	13	26	57
$t_{1/2}$ [h]	35	27	9

THERAPEUTIC INDICATIONS

Levoget (Levofloxacin) I.V. infusion is indicated in adults for the treatment of the following infections:

1. Community-acquired pneumonia
2. Complicated skin and soft tissue infections/Complicated skin and skin structure infections.

In complicated skin and soft tissue infections, Levoget (Levofloxacin) I.V. infusion should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.

3. Acute pyelonephritis
4. Complicated urinary tract infections
5. Chronic bacterial prostatitis
6. Inhalation Anthrax: post-exposure prophylaxis and curative treatment

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

DOSAGE AND ADMINISTRATION

Levoget (Levofloxacin) I.V. infusion is administered by slow intravenous infusion once or twice daily. The dosage depends in the type and severity of the infection and the susceptibility of the presumed causative pathogen. Treatment after the initial use of the Levoget (Levofloxacin) I.V. preparation may be completed with an appropriate oral Levoget (Levofloxacin) Tablets presentation, and as considered appropriate for the individual patient.

The following dose recommendations can be given for Levoget (Levofloxacin) I.V. infusion:

A. Dosage in patients with normal renal function (creatinine clearance > 50 ml/min)

Indication	Daily dose regimen (according to severity)	Total duration of treatment[1] *(according to severity)*
Community-acquired pneumonia	500 mg once or twice daily	7 - 14 days
Complicated Skin and soft tissue infections	500 mg once or twice daily	7 - 14 days
Acute pyelonephritis	500 mg once daily	7 - 10 days
Complicated urinary tract infections	500 mg[1] once daily	7 - 14 days
Chronic bacterial prostatitis	500 mg once daily	28 days
Inhalation Anthrax	500 mg once daily	8 weeks

[1] Treatment duration includes intravenous plus oral treatment. The time to switch from intravenous to oral treatment depends on the clinical situation, but is normally 2 to 4 days.

Special Population

B. Patients with Impaired renal function (creatinine clearance ≤ 50 ml/min)

Creatinine clearance	Dosage regimen		
	250 mg/24 h	500 mg/24 h	500 mg/12 h
	First dose: 250 mg	First dose: 500 mg	First dose: 500 mg
50-20 ml/min	Then:125 mg/24h	Then: 250 mg/24 h	Then:250 mg/12 h
19-10 ml/min	Then: 125 mg/48 h	Then: 125 mg/24 h	Then:125 mg/12 h
< 10 ml/min (including haemodialysis and CAPD)[1]	Then: 125 mg/48 h	Then: 125 mg/24 h	Then:125 mg/24 h

[1] No additional doses are required after hemodialysis or continuous ambulatory peritoneal dialysis (CAPD).

Method of administration

Levoget (Levofloxacin) I.V. infusion is only intended for slow intravenous infusion; it is administered once or twice daily. The infusion time must be at least 30 minutes for 250 mg or 60 minutes for 500 mg Levoget (Levofloxacin) I.V. infusion.

Adverse Reactions:

Common: Insomnia, Headache, Dizziness, Diarrhea, Vomiting, Nausea, Hepatic enzyme Increased (ALT/AST, alkaline phosphatase, GGT), Phlebitis, Infusion site reaction (Pain and reddening).

Uncommon: Fungal infection including Candida infection Pathogen resistance, Leukopenia Eosinophilia, Anorexia, Anxiety, Confusional state, Nervousness, Somnolence, Tremor, Dysgeusia, Vertigo, Dyspnea, Abdominal pain, Dyspepsia, Flatulence, Constipation, Blood bilirubin, Increased, Rash, Pruritus, Urticaria, Hyperhidrosis, Arthralgia, Myalgia, Blood creatinine increased, Asthenia.

Rare: Thrombocytopenia, Neutropenia, Angioedema, Hypersensitivity, Hypoglycaemia, particularly in diabetic patients, Psychotic reactions (with e.g. hallucination, paranoia), Depression, Agitation, Abnormal dreams, Nightmares, Convulsion, Paraesthesia, Visual disturbances such as blurred vision, Tinnitus, Tachycardia, Palpitation, Hypotension, Tendon disorders including tendinitis (e.g. Achilles tendon), Muscular weakness which may be of special importance in patients with myasthenia gravis, Renal failure acute (e.g. due to interstitial nephritis), Pyrexia.

Frequency Not Known: Pancytopenia, Agranulocytosis, Hemolytic anemia, Anaphylactic shock Anaphylactoid shock, Hyperglycemia, Hypoglycemic coma, Psychotic disorders with self-endangering behavior including suicidal ideation or suicide attempt, Peripheral sensory neuropathy, Peripheral sensory motor neuropathy, Parosmia including anosmia, Dyskinesia, Extrapyramidal disorder, Ageusia, Syncope, Benign intracranial, hypertension, Transient vision loss, Hearing loss, Hearing impaired, Ventricular tachycardia, which may result in cardiac arrest, Ventricular arrhythmia and torsade de pointes (reported predominantly in patients with risk factors of QT prolongation), electrocardiogram QT prolonged, Bronchospasm, Pneumonitis allergic, Diarrhoea – haemorrhagic which in very rare cases may be indicative of enterocolitis, including pseudomembranous colitis, Pancreatitis, Jaundice and severe liver injury, including fatal cases with acute liver failure, primarily in patients with severe underlying diseases, Hepatitis, Toxic epidermal necrolysis Stevens-Johnson syndrome, Erythema multiforme, Photosensitivity reaction, Leukocytoclastic vasculitis, Stomatitis, Rhabdomyolysis, Tendon rupture (e.g. Achilles tendon), Ligament rupture, Muscle rupture, Arthritis, Pain (including pain in back, chest, and extremities).

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

Contraindications

Levofloxacin Solution for infusion must not be used:

- in patients hypersensitive to levofloxacin or other quinolones or to any of the excipients.
- in patients with epilepsy
- in patients with history of tendon disorders related to fluoroquinolone administration
- in children or growing adolescents
- during pregnancy
- in breast-feeding women.

WARNING

Floroquinolones, including levofloxacin are associated with an increased risk of tendinitis and tendon rupture in all ages. This risk is further increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants.

PRECAUTIONS

General

- No fluoroquinolone should be co-administered with any solution containing multivalent cations, e.g., magnesium, through the same intravenous.

- Stop treatment with a fluoroquinolone antibiotic, levofloxacin, at the first sign of a side effect involving muscles, tendons or joints and the nervous system. Fluoroquinolone antibiotics, levofloxacin, should not be used:
  - 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
- Fluoroquinolones should generally be avoided in patients who have previously had serious side effects with a fluoroquinolone or quinolone antibiotic.
- Fluoroquinolones should be used with special caution in the elderly, patients with kidney disease and those who have had an organ transplantation because these patients are at a higher risk of tendon injury. Since the use of a corticosteroid with a fluoroquinolone also increases this risk, combined use of these medicines should be avoided.

The use of levofloxacin should be avoided in patients who have experienced serious adverse reactions in the past when using quinolone or fluoroquinolone containing products. Treatment of these patients with Levofloxacin should only be initiated in the absence of alternative treatment options and after careful benefit/risk assessment.

Prolonged, disabling and potentially irreversible serious adverse drug reactions
Very rare cases of prolonged (continuing months or years), disabling and potentially irreversible serious adverse drug reactions affecting different, sometimes multiple, body systems (musculoskeletal, nervous, psychiatric and senses) have been reported in patients receiving quinolones and fluoroquinolones irrespective of their age and pre-existing risk factors. Levofloxacin should be discontinued immediately at the first signs or symptoms of any serious adverse reaction and patients should be advised to contact their prescriber for advice.

Methicillin-resistant Staphylococcus aureus (MRSA)
Methicillin-resistant S. aureus are very likely to possess co-resistance to fluoroquinolones, including levofloxacin. Therefore, levofloxacin is not recommended for the treatment of known or suspected MRSA infections unless laboratory results have confirmed susceptibility of the organism to levofloxacin (and commonly recommended antibacterial agents for the treatment of MRSA-infections are considered inappropriate).
Prescribers are advised to take into account the local prevalence of resistance in E. coli (common pathogen involved in urinary tract infections) to fluoroquinolones.

Inhalation Anthrax
Use in humans is based on in vitro Bacillus anthracis susceptibility data and on animal experimental data together with limited human data. Treating physicians should refer to national and/or international consensus documents regarding the treatment of anthrax.

Infusion time
The recommended infusion time of at least 30 minutes for 250 mg or 60 minutes for 500 mg levofloxacin should be observed. It is known for ofloxacin, that during infusion tachycardia and a temporary decrease in blood pressure may develop. In rare cases, as a consequence of a profound drop in blood pressure, circulatory collapse may occur. Should a conspicuous drop in blood pressure occur during infusion of levofloxacin, (l-isomer of ofloxacin) the infusion must be halted immediately.

Sodium content
Levoget (Levofloxacin) I.V. infusion contains 900 mg sodium per 100 ml dose. To be taken into consideration by patients on a controlled sodium diet.

Tendinitis and tendon rupture
Tendinitis and tendon rupture (especially but not limited to Achilles tendon), sometimes bilateral, may occur as early as within 48 hours of starting treatment with quinolones and fluoroquinolones and have been reported to occur even up to several months after discontinuation of treatment. The risk of tendinitis and tendon rupture is increased in older patients, patients with renal impairment, patients with solid organ transplants, in patients receiving daily doses of 1000 mg levofloxacin and those treated concurrently with corticosteroids. Therefore, concomitant use of corticosteroids should be avoided. The daily dose should be adjusted in elderly patients based on creatinine clearance.
At the first sign of tendinitis (e.g. painful swelling, inflammation) the treatment with Levofloxacin should be discontinued and alternative treatment should be considered. The affected limb(s) should be appropriately treated (e.g. immobilization). Corticosteroids should not be used if signs of tendinopathy occur.

Clostridium difficile-associated disease
Diarrhea, particularly if severe, persistent and/or bloody, during or after treatment with Levofloxacin (including several weeks after treatment), may be symptomatic of Clostridium difficile-associated disease (CDAD). CDAD may range in severity from mild to life threatening, the most severe form of which is pseudomembranous colitis. It is therefore, important to consider this diagnosis in patients who develop serious diarrhea during or after treatment with levofloxacin. If CDAD is suspected or confirmed, Levofloxacin should be stopped immediately and appropriate treatment initiated without delay (e.g. oral metronidazole or vancomycin). Medicinal products inhibiting the peristalsis are contraindicated in this clinical situation.

Patients predisposed to seizures
Quinolones may lower the seizure threshold and may trigger seizures. Levofloxacin is contraindicated in patients with a history of epilepsy and, as with other quinolones, should be used with extreme caution in patients predisposed to seizures, or concomitant treatment with active substances that lower the cerebral seizure threshold, such as theophylline.
In case of convulsive seizures, treatment with levofloxacin should be discontinued.

Patients with G-6- phosphate dehydrogenase deficiency
Patients with latent or actual defects in glucose-6-phosphate dehydrogenase activity may be prone to hemolytic reactions when treated with quinolone antibacterial agents. Therefore, if levofloxacin has to be used in these patients, potential occurrence of hemolysis should be monitored.

Patients with renal impairment
Since levofloxacin is excreted mainly by the kidneys, the dose of Levofloxacin should be adjusted in patients with renal impairment.

Hypersensitivity reactions
Levofloxacin can cause serious, potentially fatal hypersensitivity reactions (e.g. angioedema to anaphylactic shock), occasionally following the initial dose. Patients should discontinue treatment immediately and contact their physician, who will initiate appropriate emergency measures.

Severe bullous reactions
Cases of severe bullous skin reactions, such as Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported with Levofloxacin. Patients should be advised to contact their doctor immediately prior to continuing treatment if skin and/or mucosal reactions occur.

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

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

Patients treated with Vitamin K antagonists
Due to possible increase in coagulation tests (PT/INR) and/or bleeding in patients treated with levofloxacin in combination with a vitamin K antagonist (e.g. warfarin), coagulation tests should be monitored when these drugs are given concomitantly.

Psychotic reactions
Psychotic reactions have been reported in patients receiving quinolones, including levofloxacin. In very rare cases these have progressed to suicidal thoughts and self-endangering behavior- sometimes after only a single dose of levofloxacin. In the event that the patient develops these reactions, levofloxacin should be discontinued and appropriate measures instituted. Caution is recommended if levofloxacin is to be used in psychotic patients or in patients with a history of psychiatric disease.

QT interval prolongation
Caution should be taken when using fluoroquinolones, including levofloxacin, in patients with known risk factors for prolongation of the QT interval such as, for example:
- congenital long QT syndrome
- concomitant use of drugs that are known to prolong the QT interval (e.g. Class IA and III antiarrhythmics, tricyclic antidepressants, macrolides, antipsychotics).
- uncorrected electrolyte imbalance (e.g. hypokalemia, hypomagnesemia)
- cardiac disease (e.g. heart failure, myocardial infarction, bradycardia)

Elderly patients and women may be more sensitive to QTc-prolonging medications. Therefore, caution should be taken when using fluoroquinolones, including levofloxacin, in these populations.

Peripheral neuropathy
Cases of sensory or sensorimotor polyneuropathy resulting in paraesthesia, hypaesthesia, dysesthesia, or weakness have been reported in patients receiving quinolones and fluoroquinolones.
Patients under treatment with Levofloxacin should be advised to inform their doctor prior to continuing treatment if symptoms of neuropathy such as pain, burning, tingling, numbness, or weakness develop in order to prevent the development of potentially irreversible condition.

Hepatobiliary disorders
Cases of hepatic necrosis up to fatal hepatic failure have been reported with levofloxacin, primarily in patients with severe underlying diseases, e.g. sepsis. Patients should be advised to stop treatment and contact their doctor if signs and symptoms of hepatic disease develop such as anorexia, jaundice, dark urine, pruritus or tender abdomen.

Exacerbation of myasthenia gravis
Fluoroquinolones, including levofloxacin, have neuromuscular blocking activity and may exacerbate muscle weakness in patients with myasthenia gravis. Postmarketing serious adverse reactions, including deaths and the requirement for respiratory support, have been associated with fluoroquinolone use in patients with myasthenia gravis. Levofloxacin is not recommended in patients with a known history of myasthenia gravis.

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

Superinfection
The use of levofloxacin, especially if prolonged, may result in overgrowth of non-susceptible organisms. If superinfection occurs during therapy, appropriate measures should be taken.

Vascular disorders
There is an increased risk of aortic aneurysm and dissection after intake of fluoroquinolones, particularly in the older population. 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 preexisting 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.

Interference with laboratory tests
In patients treated with levofloxacin, determination of opiates in urine may give false-positive results. It may be necessary to confirm positive opiate screens by more specific method.
Levofloxacin may inhibit the growth of Mycobacterium tuberculosis and, therefore, may give false-negative results in the bacteriological diagnosis of tuberculosis.

Pregnancy
There are limited amount of data with respect to the use of levofloxacin in pregnant women. Therefore, levofloxacin must not be used in pregnant women.

Nursing Mother
Levofloxacin is contraindicated in breast-feeding women.

Drug Interactions
Effect of other medicinal products on levofloxacin

Theophylline, fenbufen or similar non-steroidal anti-inflammatory drugs
No pharmacokinetic interactions of levofloxacin were found with theophylline in a clinical study. However, a pronounced lowering of the cerebral seizure threshold may occur when quinolones are given concurrently with theophylline, nonsteroidal anti-inflammatory drugs, or other agents which lower the seizure threshold. Levofloxacin concentrations were about 13 % higher in the presence of fenbufen than when administered alone.

Probenecid and cimetidine
Probenecid and cimetidine had a statistically significant effect on the elimination of levofloxacin. The renal clearance of levofloxacin was reduced by cimetidine (24 %) and probenecid (34 %). This is because both drugs are capable of blocking the renal tubular secretion of levofloxacin. Caution should be exercised when levofloxacin is co-administered with drugs that effect the tubular renal secretion such as probenecid and cimetidine, especially in renally impaired patients.

Other relevant information
Clinical pharmacology studies have shown that the pharmacokinetics of levofloxacin were not affected to any clinically relevant extent when levofloxacin was administered together with the following drugs:
- calcium carbonate
- digoxin
- glibenclamide
- ranitidine.

Effect of levofloxacin on other medicinal products
Ciclosporin
The half-life of ciclosporin was increased by 33 % when co-administered with levofloxacin.

Vitamin K antagonists
Increased coagulation tests (PT/INR) and/or bleeding, which may be severe, have been reported in patients treated with levofloxacin in combination with a vitamin K antagonist (e.g. warfarin). Coagulation tests, therefore, should be monitored in patients treated with vitamin K antagonists.

Drugs known to prolong the QT interval
Levofloxacin, like other fluoroquinolones, should be used with caution in patients receiving drugs known to prolong the QT interval (e.g. Class IA and III antiarrhythmics, tricyclic antidepressants, macrolides, antipsychotic).

Other relevant information
In a pharmacokinetic interaction study, levofloxacin did not affect the pharmacokinetics of theophylline (which is a probe substrate for CYP1A2), indicating that levofloxacin is not a CYP1A2 inhibitor.

Effects on ability to drive and use machines
Some undesirable effects (e.g. dizziness/vertigo, drowsiness, visual disturbances) may impair the patient's ability to concentrate and react, and therefore may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

OVERDOSAGE
The most important signs to be expected following acute overdosage of levofloxacin are central nervous system symptoms such as confusion, dizziness, impairment of consciousness, and convulsive seizures, increases in QT interval as well as gastro-intestinal reactions such as nausea and mucosal erosions. CNS effects including confusional state, convulsion, hallucination, and tremor have been observed in post marketing experience.

In the event of overdose, symptomatic treatment should be implemented. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation. Antacids may be used for protection of gastric mucosa. Hemodialysis, including peritoneal dialysis and Continuous Ambulatory Peritoneal Dialysis (CAPD), are not effective in removing levofloxacin from the body. No specific antidote exists.

HOW SUPPLIED
Levoget (Levofloxacin) I.V. 500mg is available in 1x100mL vial.
Levoget (Levofloxacin) I.V. 750mg is available in 1x150mL vial.

STORAGE
Do not store above 30°C.
Do not refrigerate.
Protect from sunlight.
Once the vial is removed from the carton the infusion solution must be used within three days.
Once the vial has been opened, the infusion solution must be used within three hours.
The expiration date refers to the product correctly stored at the required conditions.
Keep in the pack until required.

Keep out of the reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Manufactured by:

Getz pharma (PVT) LIMITED
www.getzpharma.com

29-30, Sector-27,
Korangi Industrial Area,
Karachi, Pakistan.

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