For the use of a registered medical practitioner or a Hospital or a Laboratory only

LEVOFLOXACIN INFUSION IP 500mg/100mL

NIRLIV®*

Therapeutic Category: Antibacterial agent

WARNING:
Fluoroquinolones, 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 [See Warnings and Precaution].

Fluoroquinolones, including Levofloxacin, may exacerbate muscle weakness in persons with myasthenia gravis.
Avoid Levofloxacin in patients with a known history of myasthenia gravis [See Warnings and Precautions].

COMPOSITION:
Each 100 mL contains
Levofloxacin Hemihydrate IP
Equivalent to Levofloxacin 500 mg
Water for Injections IP q. s.

DESCRIPTION:
Levofloxacin is a synthetic broad-spectrum fluoroquinolone antibacterial agent for IV administration. Its empirical formula is $C_{18}H_{20}FN3041/2H_2O$ and its molecular weight is 370.38. It is the L-isomer of the racemate, Ofloxacin, and a quinolone anti microbial agent. The antibacterial activity in ofloxacin resides primarily in L-isomer.
The appearance of Levofloxacin infusion may range from a clear yellow to a clear greenish-yellow solution. This does not adversely affect product potency.
Levofloxacin is a sterile, preservative-free aqueous solution of levofloxacin in Water for Injection, with pH ranging from 3.8 to 5.8.

MODE 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 mechanism of action of levofloxacin and other fluoroquinolone antimicrobials involves inhibition of bacterial topoisomerase IV and DNA gyrase (both of which are type II topoisomerases), enzymes required for DNA replication, transcription, repair and recombination.

PHARMACOKINETICS:
Absorption
Oral & intravenous administration levofloxacin is rapidly and almost completely absorbed with peak

plasma Concentration being obtained within 1 hr. The mean ± SD peak plasma concentration attained was 6.2 ± 1.0 mcg/mL after a 500 mg dose infused over 60 minutes and 11.5 ± 4.0 mcg/mL after a 750 mg dose infused over 90 minutes. The absolute bioavaibility is approximately 100%. Levofloxacin obeys linear Pharmacokinetics over a range of 50 to 600 mg. Steady-state conditions are reached within 48 hours following a 500 mg or 750 mg once-daily dosage regimen. The mean ± SD peak and trough plasma concentrations attained following multiple once-daily IV regimens were approximately 6.4 ± 0.8 and 0.6 ± 0.2 mcg/mL after the 500 mg doses, and 12.1 ± 4.1 and 1.3 ± 0.71 mcg/mL after the 750 mg doses, respectively. Food has little or no effect on the absorption of Levofloxacin. The oral and IV routes of administration can be considered interchangeable.

Distribution

Levofloxacin is widely distributed into body tissues. Levofloxacin reaches its peak levels in skin tissues and in blister fluid of healthy subjects at approximately 3 hours after dosing. Steady state is achieved within 3 days. The skin tissue biopsy to plasma AUC ratio is approximately 2 and the blister fluid to plasma AUC ratio is approximately 1 following multiple once-daily oral administrations of 750 mg and 500 mg doses of Levofloxacin, respectively, to healthy subjects. Levofloxacin also penetrates well 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. Approximately 30-40% of Levofloxacin is bound to serum protein. Levofloxacin is mainly bound to serum albumin in humans. 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. It metabolized to a very small extent. The metabolites being desmethyl Levofloxacin and Levofloxacin N-oxide. These metabolites account for < 5 % of the dose excreted in urine.

Elimination

The excretion is primarily by renal route (> 85% of the administered dose). Levofloxacin is excreted largely 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 or intravenously. Levofloxacin is eliminated relatively slowly from the plasma (t =6-8 hrs). The mean apparent total body clearance and renal clearance range from approximately 144 to 226 mL/min and 96 to 142 mL/min, respectively. Renal clearance in excess of the glomerular filtration rate suggests that tubular secretion of levofloxacin occurs in addition to its glomerular filtration. Concomitant administration of either cimetidine or probenecid results in approximately 24% and 35% reduction in the levofloxacin renal clearance, respectively, indicating that secretion of levofloxacin occurs in the renal proximal tubule.

There are no major differences in the Pharmacokinetics of Levofloxacin following oral and intravenous administration.

Geriatric

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.

Pediatrics
As per literature reviewed, pediatric patients cleared levofloxacin faster than adult patients, resulting in lower plasma exposures than adults for a given mg/kg dose. Dosage regimen of 8 mg/kg every 12 hours (not to exceed 250 mg per dose) for pediatric patients 6 months to 17 years of age would achieve comparable steady state plasma exposures (AUC0-24 and Cmax) to those observed in adult patients administered 500 mg of levofloxacin once every 24 hours.

Gender
There are no significant differences in levofloxacin pharmacokinetics between male and female subjects when subjects' 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 the race of the subjects.

Renal Impairment
Clearance of levofloxacin is substantially reduced and plasma elimination half-life is substantially prolonged in adult patients with impaired renal function (creatinine clearance < 50 mL/min), requiring dosage adjustment in such patients to avoid accumulation. Neither hemodialysis nor continuous ambulatory peritoneal dialysis (CAPD) is effective in removal of levofloxacin from the body, indicating that supplemental doses of Levofloxacin are not required following hemodialysis or CAPD.

MICROBIOLOGY:
Levofloxacin has been shown to be active against most isolates of the following bacteria.

Gram-positive microorganisms:	**Gram-negative microorganisms:**	**Other Microorganisms:**
Enterococcus faecalis (many strains are only moderately susceptible) Staphylococcus aureus (methicillin susceptible strains) Staphylococcus epidermidis Staphylococcus saprophyticus Streptococcus pneumoniae (Including penicillin Resistant strains) Streptococcus pyrogenes	Enterobacter cloacae Escherichia coli Haemophilus infulenzae Haemophilus parainfluenzae Klebsiella pneumoniae Legionella pneumophila Moraxella catarrhalis Proteus mirabilis Pseudomonas aeruginosa Serratia marcescens As with other drugs in this class, some strains of Pseudomonas aeruginosa may develop resistance fairly rapidly during treatment with Levofloxacin.	Chlamydia pneumoniae Mycoplasma pneumonia

INDICATIONS:

- Nosocomial Pneumonia
- Community-Acquired Pneumonia (CAP)
- Acute Bacterial Sinusitis
- Acute Bacterial Exacerbation of Chronic Bronchitis (AECB)
- Complicated / Uncomplicated Skin and Skin Structure Infections
- Chronic Bacterial Prostatitis
- Complicated / Uncomplicated Urinary Tract Infections
- Acute Pyelonephritis
- Suspected Bacteraemia: due to intra-abdominal infection/infected intravascular device/ pneumonia / RTI / SSSI / post-surgery (including post caesarean) / sepsis of unknown source
- Inhalational Anthrax (Post-Exposure) - The safety of Levofloxacin in adults for durations of therapy beyond 28 days or in pediatric patients for durations of therapy beyond 14 days has not been studied. Prolonged Levofloxacin therapy should only be used when the benefit outweighs the risk
- Plague- Levofloxacin is indicated for treatment of plague, including pneumonic and septicemic plague, due to Yersinia pestis (Y. pestis) and prophylaxis for plague in adults and pediatric patients, 6 months of age and older.

DOSAGE AND ADMINISTRATION:

Levofloxacin Infusion should only be administered by intravenous infusion. It is not for intramuscular, intrathecal, intraperitoneal or subcutaneous administration. It should be infused intravenously slowly over a period of not less than 60 minutes, depending on the dosage.

Duration of treatment

The duration of therapy varies according to the cause of the disease. The administration of Levofloxacin should be continued for a minimum of 48 to 72 hrs after the patient has become afebrile or evidence of bacterial eradication has been obtained.

DOSAGE ADJUSTMENT IN ADULT PATIENT WITH NORMAL RENAL FUNCTION:

Table 1. Dosage in Adult Patients with Normal Renal Function (creatinine clearance ≥ 50mL/min)

Type of Infection	**Dosed Every 24 Hours**	**Duration (days)†**
Nosocomial Pneumonia	750 mg	7–14
Community Acquired Pneumonia‡	500 mg	7–14
Community Acquired Pneumonia§	750 mg	5
Acute Bacterial Sinusitis	750 mg	5
	500 mg	10–14
Acute Bacterial Exacerbation of Chronic Bronchitis	500 mg	7
Complicated Skin and Skin Structure Infections (SSSI) Uncomplicated (SSSI)	750 mg 500 mg	7–14 7–10
Chronic Bacterial Prostatitis	500 mg	28
Complicated Urinary tract Infection (cUTI) or Acute Pyelonephritis (AP)¶	750 mg	5
Complicated Urinary Tract Infection (cUTI) or Acute Pyelonephritis (AP)#	250 mg	10
Uncomplicated Urinary Tract Infection	250 mg	3
Inhalational Anthrax (Post-Exposure), adult and		

pediatric patients > 50 kg Þ,ß Pediatric patients < 50 kg and ≥ 6 months of ageÞ,ß	500mg see Pediatric Dose	60ß 60ß
Plague, adult and pediatric patients > 50 kg à Pediatric patients < 50 kg and ≥ 6 months of age	500mg see Pediatric Dose	10 to 14 10 to 14

† Sequential therapy (intravenous to oral) may be instituted at the discretion of the physician.
‡ Due to methicillin-susceptible Staphylococcus aureus, Streptococcus pneumoniae (including multi-drug-resistant isolates [MDRSP]), Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Moraxella catarrhalis, Chlamydophila pneumoniae, Legionella pneumophila, or Mycoplasma pneumoniae.
§ Due to Streptococcus pneumoniae (excluding multi-drug-resistant isolates [MDRSP]), Haemophilus influenzae, Haemophilus parainfluenzae, Mycoplasma pneumoniae, or Chlamydophila pneumoniae.
¶ This regimen is indicated for cUTI due to Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis and AP due to E. coli, including cases with concurrent bacteremia.
# This regimen is indicated for cUTI due to Enterococcus faecalis, Enterococcus cloacae, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa; and for AP due to E. coli.
Þ Drug administration should begin as soon as possible after suspected or confirmed exposure to aerosolized B. anthracis. This indication is based on a surrogate endpoint. Levofloxacin plasma concentrations achieved in humans are reasonably likely to predict clinical benefit.
ß The safety of Levofloxacin in adults for durations of therapy beyond 28 days or in pediatric patients for durations beyond 14 days has not been studied. An increased incidence of musculoskeletal adverse events compared to controls has been observed in pediatric patients. Prolonged Levofloxacin therapy should only be used when the benefit outweighs the risk.
à Drug administration should begin as soon as possible after suspected or confirmed exposure to Yersinia pestis. Higher doses of Levofloxacin typically used for treatment of pneumonia can be used for treatment of plague, if clinically indicated.

Dosage in Pediatric Patients
Table 2. Dosage in Pediatric Patients ≥ 6 months of age

Type of Infection*	Dose	Freq. Once every	Duration†
Inhalational Anthrax (post-exposure)‡,§			
Pediatric patients > 50 kg	500 mg	24 hr	60 days§
Pediatric patients < 50 kg			
and ≥ 6 months of age	8 mg/kg (not to exceed 250 mg per dose)	12 hr	60 days§
Plague¶			
Pediatric patients > 50 kg	500 mg	24 hr	10 to 14 days
Pediatric patients < 50 kg and ≥ 6 months of age	8 mg/kg (not to exceed 250 mg per dose)	12 hr	10 to 14 days

* Due to Bacillus anthracis [see Indications and Usage (1.13)] and Yersinia pestis [see Indications and Usage (1.14)].

† Sequential therapy (intravenous to oral) may be instituted at the discretion of the physician.
‡ Drug administration should begin as soon as possible after suspected or confirmed exposure to aerosolized B. anthracis. This indication is based on a surrogate endpoint. Levofloxacin plasma concentrations achieved in humans are reasonably likely to predict clinical benefit.
§ The safety of Levofloxacin in pediatric patients for durations of therapy beyond 14 days has not been studied. An increased incidence of musculoskeletal adverse events compared to controls has been observed in pediatric patients. Prolonged Levofloxacin therapy should only be used when the benefit outweighs the risk.
¶ Drug administration should begin as soon as possible after suspected or confirmed exposure to Yersinia pestis.

Dosage Adjustment in Adult with Renal Impairment

Table 3. Dosage Adjustment in Adult Patient s with Renal Impairment (creatinine clearance <50 mL/min)

Dosage in Normal Renal Function Every 24 hours	**Creatinine Clearance 20 to 49 mL/min**	**Creatinine Clearance 10 to 19 mL/min**	**Hemodialysis or Chronic Ambulatory Peritoneal Dialysis (CAPD)**
750 mg	750 mg every 48 hours	750 mg initial dose, then 500 mg every 48 hours	750 mg initial dose, then 500 mg every 48 hours
500 mg	500 mg initial dose, then 250 mg every 24 hours	500 mg initial dose, then 250 mg every 48 hours	500 mg initial dose, then 250 mg every 48 hours
250 mg	No dosage adjustment required	250 mg every 48 hours. If treating uncomplicated UTI, then no dosage adjustment is required	No information on dosing adjustment is available

Dosage in Geriatric Patients

No adjustment is required for the elder patient, as the liver does not metabolize Levofloxacin.

Administration Instruction

Caution: Rapid or bolus intravenous infusion of Levofloxacin has been associated with hypotension and must be avoided. Levofloxacin should be administered only by intravenous infusion.

Levofloxacin should not be co-administered with any solution containing multivalent cations, e.g., magnesium, through the same intravenous line.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Because only limited data are available on the compatibility of Levofloxacin with other intravenous substances, additives or other medications should not be added to Levofloxacin. If the same intravenous line is used for sequential infusion of several different drugs, the line should be flushed before and after infusion of Levofloxacin with an infusion solution compatible with Levofloxacin and with any other drug(s) administered via this common line.

Since the infusions are for single-use only, any unused portion remaining in the vial should be discarded.

CONTRAINDICATIONS:

Levofloxacin is contraindicated in persons with known hypersensitivity to levofloxacin or other quinolone antibacterials.

In patients with epilepsy, myasthenia gravis and history of tendon disorders related to fluoroquinolone administration

During pregnancy and in breast feeding women.

WARNINGS AND PRECAUTIONS:

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

Exacerbation of Myasthenia Gravis- Fluoroquinolones, including Levofloxacin have neuromuscular blocking activity and may exacerbate muscle weakness in persons with myasthenia gravis. Some serious adverse events, including deaths and requirement for ventilatory support, may be associated with fluoroquinolone use in persons with myasthenia gravis. Avoid Levofloxacin in patients with a known history of myasthenia gravis

Hypersensitivity Reactions- Serious and occasionally fatal hypersensitivity and/or anaphylactic reactions may occur in patients receiving therapy with Fluoroquinolones, 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. Levofloxacin 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.

Other Serious and Sometimes Fatal Reactions- As per Literature reviewed, other serious and sometimes fatal events, due to hypersensitivity, and uncertain etiology, have been reported rarely in patients receiving therapy with fluoroquinolones, 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; 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 drug should be discontinued immediately at the first appearance of skin rash, jaundice, or any other sign of hypersensitivity and supportive measures instituted.

Hepatotoxicity- As per literature reviewed, severe hepatotoxicity have been reported within 14 days of initiation of therapy and in most cases within 6 days. The majority of fatal hepatotoxicity may occur in patients 65 years of age or older. Levofloxacin should be discontinued immediately if the patient develops any signs and symptoms of hepatitis.

Central Nervous System Effects- Fluoroquinolones may also cause central nervous system stimulation which may lead to tremors, restlessness, anxiety, lightheadedness, confusion, 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 Levofloxacin, the drug should be discontinued and appropriate measures must be instituted. As with other fluoroquinolones, Levofloxacin 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).

Clostridium difficile- Associated Diarrhea- Clostridium difficile-associated diarrhea (CDAD) may occur with use of nearly all antibacterial agents, including Levofloxacin and may range in severity from mild diarrhea to fatal colitis. CDAD must be considered in all patients, who present with diarrhea following antibiotic use. Careful medical history is necessary, since CDAD may occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

Peripheral Neuropathy- Rare cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesias, hypoesthesias, dysesthesias and weakness have occur in patients receiving fluoroquinolones. Levofloxacin should be discontinued, if the patient experiences symptoms of neuropathy including pain, burning, tingling, numbness, and/or weakness or other alterations of sensation including light touch, pain, temperature, position sense, and vibratory sensation in order to prevent the development of an irreversible condition.

Prolongation of the QT Interval- Some fluoroquinolones, including Levofloxacin, may be associated with prolongation of the QT interval on the electrocardiogram and infrequent cases of arrhythmia. Levofloxacin should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia, and patients receiving Class IA (quinidine, procainamide), or Class III (amiodarone, sotalol) antiarrhythmic agents. Elderly patients may be more susceptible to drug-

associated effects on the QT interval.

Musculoskeletal Disorders in Pediatric Patients and Arthropathic Effects in Animals- As Per literature reviewed, An increased incidence of musculoskeletal disorders like arthralgia, arthritis, tendinopathy, and gait abnormality have been observed on patients receiving Levofloxacin.

Blood Glucose Disturbances- As per literature reviewed, disturbances of blood glucose, including symptomatic hyper- and hypoglycemia, have been reported with Levofloxacin, like other fluoroquinolones, usually in diabetic patients receiving concomitant treatment with an oral hypoglycemic agent (e.g., glyburide) or with insulin.

Photosensitivity/Phototoxicity- Moderate to severe photosensitivity/phototoxicity reactions, the latter of which may manifest as exaggerated sunburn reactions can be associated with the use of fluoroquinolones after sun or UV light exposure. Therefore, excessive exposure to these sources of light should be avoided. Drug therapy should be discontinued, if photosensitivity/phototoxicity occurs.

Development of Drug Resistant Bacteria- Use of Levofloxacin in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Carcinogenesis, Mutagenesis, Impairment of Fertility- As per literature reviewed, In a lifetime bioassay in rats, levofloxacin exhibited no carcinogenic potential following daily dietary administration for 2 years; the highest dose (100 mg/kg/day) was 1.4 times the highest recommended human dose (750 mg) based upon relative body surface area. Levofloxacin was not mutagenic in the following assays: Ames bacterial mutation assay (S. typhimurium and E. coli), CHO/HGPRT forward mutation assay, mouse micronucleus test, mouse dominant lethal test, rat unscheduled DNA synthesis assay, and the mouse sister chromatid exchange assay. It was positive in the in vitro chromosomal aberration (CHL cell line) and sister chromatid exchange (CHL/IU cell line) assays. Levofloxacin caused no impairment of fertility or reproductive performance in rats at oral doses as high as 360 mg/kg/day, corresponding to 4.2 times the highest recommended human dose based upon relative body surface area and intravenous doses as high as 100 mg/kg/day, corresponding to 1.2 times the highest recommended human dose based upon relative body surface area.

ADVERSE REACTIONS:

- Tendon Effects **[see Warnings and Precautions]**
- Exacerbation of Myasthenia Gravis **[see Warnings and Precautions]**
- Hypersensitivity Reactions **[see Warnings and Precautions]**
- Other Serious and Sometimes Fatal Reactions **[see Warnings and Precautions]**
- Hepatotoxicity **[see Warnings and Precautions]**
- Central Nervous System Effects **[see Warnings and Precautions]**
- Clostridium difficile-Associated Diarrhea **[see Warnings and Precautions]**
- Peripheral Neuropathy **[see Warnings and Precautions]**
- Prolongation of the QT Interval **[see Warnings and Precautions]**
- Musculoskeletal Disorders in Pediatric Patients **[see Warnings and Precautions]**
- Blood Glucose Disturbances **[see Warnings and Precautions]**
- Photosensitivity/Phototoxicity **[see Warnings and Precautions]**

- Development of Drug Resistant Bacteria **[see Warnings and Precautions]**
- Hypotension may occur with rapid or bolus intravenous infusion of Levofloxacin. Levofloxacin should be infused slowly over 60 to 90 minutes, depending on dosage.
- Crystalluria and cylindruria may occur with quinolones, including Levofloxacin. Therefore, adequate hydration of patients receiving Levofloxacin should be maintained to prevent the formation of highly concentrated urine.

It is well tolerated. Most adverse effects are transient in duration and mild to moderate in severity. After IV infusion, phlebitis and reddening at infusion site is reported. Allergic reactions like pruritus, rash, urticaria, bronchospasm, dyspnoea, and angio-oedema may occur.

DRUG INTERACTIONS:

Chelation Agents: Antacids, Sucralfate, Metal Cations, Multivitamins- There are no data concerning an interaction of intravenous fluoroquinolones with oral antacids, sucralfate, multivitamins, didanosine, or metal cations. However, no fluoroquinolone should be co-administered with any solution containing multivalent cations, e.g., magnesium, through the same intravenous line.

Warfarin- Prothrombin time, International Normalized Ratio (INR), or other suitable anticoagulation tests should be closely monitored, if Levofloxacin is administered concomitantly with warfarin. Patients should also be monitored for evidence of bleeding.

Antidiabetic Agents- As per literature reviewed, disturbances of blood glucose, including hyperglycemia and hypoglycemia, have been reported in patients treated concomitantly with fluoroquinolones and antidiabetic agents. Therefore, careful monitoring of blood glucose is recommended, when these agents are co-administered.

Theophylline- theophylline levels should be closely monitored and appropriate dosage adjustments made, when Levofloxacin is co-administered. Adverse reactions, including seizures, may occur with or without an elevation in serum theophylline levels.

Cyclosporine- no dosage adjustment is required for Levofloxacin or cyclosporine, when administered concomitantly.

Digoxin- no dosage adjustment for Levofloxacin or digoxin is required, when administered concomitantly.

Interactions with Laboratory or Diagnostic Testing- Some fluoroquinolones, 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.

USE IN SPECIFIC POPULATION:

Pregnancy- Levofloxacin should be used during pregnancy, only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers- as per literature reviewed, it is presumed that levofloxacin will 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.

Pediatric Use- Quinolones, including levofloxacin, cause arthropathy and osteochondrosis. Pediatric patients, ranging in age from six months to 16 years, clear levofloxacin faster than adult patients, resulting in lower plasma exposures than adults for a given mg/kg dose.

Inhalational Anthrax (Post-Exposure) - As per literature reviewed, Levofloxacin is indicated in pediatric patients 6 months of age and older, for inhalational anthrax (post-exposure). The risk-benefit

assessment indicates that administration of levofloxacin to pediatric patients is appropriate. The safety of levofloxacin in pediatric patients treated for more than 14 days has not been studied.

Plague – As per literature reviewed, Levofloxacin is indicated in pediatric patients, 6 months of age and older, for treatment of plague, including pneumonic and septicemic plague due to Yersinia pestis (Y. pestis) and prophylaxis for plague. The risk-benefit assessment indicates that administration of levofloxacin to pediatric patients is appropriate

OVERDOSE:

In the event of an acute overdosage, the stomach should be emptied. The patient should be observed and appropriate hydration should be maintained. Levofloxacin is not efficiently removed by hemodialysis or peritoneal dialysis.

STORAGE:

Store protected from light and moisture.

PRESENTATION:

100 mL FFS plastic bottle.

ACULIFE®

Manufactured in India by:
Aculife Healthcare Pvt. Ltd.
Sachana, Gujarat 382150, India.

* TM owners-Nirma Ltd.