Levum® IV

Rx Levofloxacin Infusion IP (With Sodium Chloride)

WARNING: SERIOUS ADVERSE REACTIONS INCLUDING TENDINITIS, TENDON RUPTURE, PERIPHERAL NEUROPATHY, CENTRAL NERVOUS SYSTEM EFFECTS AND EXACERBATION OF MYASTHENIA GRAVIS.

See full prescribing information for complete boxed warning.

Fluoroquinolones, including Levofloxacin, have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together, including:

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

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

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

Because fluoroquinolones, including Levofloxacin, have been associated with serious adverse reactions, reserve Levofloxacin for use in patients who have no alternative treatment options for the following indications:

- Uncomplicated urinary tract infection
- Acute bacterial exacerbation of chronic bronchitis
- Acute bacterial sinusitis

This drug may cause low blood sugar and mental health related side effects.

COMPOSITION

Each 100 ml contains:

Levofloxacin Hemihydrate IP

eq. to Levofloxacin.....500 mg

Sodium Chloride IP.....900 mg

Water for Injections IP.....q.s.

DOSAGE FORM

Solution for injection

THERAPEUTIC INDICATIONS

Levofloxacin infusion is a fluoroquinolone antibacterial indicated in adults (≥ 18 years of age) with infections caused by designated, susceptible bacteria.

- Pneumonia: nosocomial and community acquired.
- Acute bacterial sinusitis.
- Acute bacterial exacerbation of chronic bronchitis.
- Skin and skin structure infections.
- Complicated urinary tract infections.
- Acute pyelonephritis.

PSOLOGY AND METHOD OF ADMINISTRATION

Posology

Levofloxacin infusion should be administered by slow intravenous infusion 250 mg to 750 mg once daily depending on the type and severity of the infection or as directed by the Physician.

Duration of treatment

The duration of treatment varies according to the course of the disease. As with antibiotic therapy in general, administration of levofloxacin should be continued for a minimum of 48 to 72 hours after the patient has become afebrile or evidence of bacterial eradication has been obtained.

It is usually possible to switch from initial intravenous treatment to the oral route after a few days, according to the condition of the patient. Given the bioequivalence of the parenteral and oral forms, the same dosage can be used. Consideration should be given to increasing the dose in cases of severe infection and special attention should be paid to available information on resistance to levofloxacin before commencing therapy.

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 populations

Dosage in patients with impaired renal function (creatinine clearance ≤ 50ml/min). The dose of levofloxacin infusion should be adjusted by monitoring serum creatinine level.

Dosage in children and adolescents: Levofloxacin 5mg/ml Solution for Infusion is contraindicated in children and growing adolescents under 18 years of age.

Method of administration: For intravenous (IV) infusion only.

Levofloxacin solution for 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 250mg or 60 minutes for 500mg Levofloxacin solution for infusion. It is possible to switch from an initial intravenous application to the oral route at the same dosage after a few days, according to the condition of the patient.

The solution is to be inspected visually for particulate matter and discolouration prior to administration and should only be used if it is clear and free from particles.

CONTRAINDICATIONS

Contraindicated in patients with known hypersensitivity to the active substance, any other quinolone or to any of the excipients.

- Patients with epilepsy.
- Patients with history of tendon disorders related to fluoroquinolone administration.
- In children or growing adolescents under 18 years of age.
- During pregnancy and breast-feeding women.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Do not mix with other medications in vial or IV line.

In the most severe cases of pneumococcal pneumonia, Levofloxacin infusion may not be the optimal therapy.

Nosocomial infections due to P. aeruginosa may require combination therapy.

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).

Resistance to fluoroquinolones of *E. coli* – the most common pathogen involved in urinary tract infections – varies across the European Union. Prescribers are advised to take into account the local prevalence of resistance in *E. coli* 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.

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 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.

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 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-Danlos syndrome, Turner syndrome, Behcet'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.

In case of sudden abdominal, chest or back pain, patients should be advised to immediately consult a physician in an emergency department.

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.

Infusion Time

The recommended infusion time of at least 30 minutes for 250 mg or 60 minutes for 500mg Levofloxacin solution for infusion 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.

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, patients receiving daily doses of 1000 mg levofloxacin and those treated concurrently with corticosteroids. Therefore, concomitant use of corticosteroids should be avoided.

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. immobilisation). Corticosteroids should not be used if signs of tendinopathy occur.

Clostridium difficile-associated disease

Diarrhoea, 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 diarrhoea during or after treatment with levofloxacin If CDAD is suspected or confirmed, levofloxacin should be stopped immediately and appropriate treatment initiated without delay. Anti-peristaltic medicinal products 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 haemolytic reactions, when treated with quinolone antibacterial agents Therefore, if levofloxacin has to be used in these patients, potential occurrence of haemolysis 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 up to anaphylactic shock), occasionally following the initial dose. Patients should discontinue treatment immediately and contact their physician or an emergency physician, who will initiate appropriate emergency measures.

Severe cutaneous adverse reactions

Severe cutaneous adverse reactions (SCARs) including toxic epidermal necrolysis (TEN: also known as Lyell's syndrome), Stevens Johnson syndrome (SJS) and drug reaction with eosinophilia and systemic symptoms (DRESS), which could be life-threatening or fatal, have been reported with levofloxacin. At the time of prescription, patients should be advised of the signs and symptoms of severe skin reactions, and be closely monitored. If signs and symptoms suggestive of these reactions appear, levofloxacin should be discontinued immediately and an alternative treatment should be considered. If the patient has developed a serious reaction such as SJS, TEN or DRESS with the use of levofloxacin, treatment with levofloxacin must not be restarted in this patient at any time.

Dysglycaemia

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

Prevention of photosensitisation

Photosensitisation 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 photosensitisation.

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 behaviour-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 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 anti-arrhythmics, 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, hypoesthesia, 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. Post marketing 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.

Interference with laboratory test

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.

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.

Levofloxacin infusion contains sodium, to be taken into consideration by patients on a controlled sodium diet and in cases where fluid restriction is required.

DRUG INTERACTIONS

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, non-steroidal 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. However, at the tested doses in the study, the statistically significant kinetic differences are unlikely to be of clinical relevance.

Caution should be exercised when levofloxacin is co-administered with drugs that affect the tubular renal secretion such as probenecid and cimetidine, especially in renally impaired patients.

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 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).

USE IN SPECIFIC POPULATIONS

Pregnancy: Reproductive studies in animals did not raise specific concern. However, in the absence of human data and due to the experimental risk of damage by fluoroquinolones to the weight-bearing cartilage of the growing organism, Levofloxacin 5mg/ml Solution for Infusion must not be used in pregnant women.

Lactation: In the absence of human data and due to the experimental risk of damage by fluoroquinolones to the weight-bearing cartilage of the growing organism, Levofloxacin solution for infusion must not be used in breast-feeding women.

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).

UNDESIRABLE EFFECTS

This drug may cause low blood sugar and mental health related side effects

Low blood sugar and mental health related side effects: The drug may cause low blood sugar and mental health related side effects. Low blood sugar levels, also called hypoglycemia, can lead to coma. The mental health side effects more prominent and more consistent across the systemic fluoroquinolone drug class. The mental health side effects reported across all the fluoroquinolones are:

- disturbances in attention,
- disorientation,
- agitation,
- nervousness,
- memory impairment,
- serious disturbances in mental abilities called delirium.

In the following table, adverse reactions are listed by system organ class and MedDRA-preferred term. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Frequencies are defined as follows:

- very common ($\geq$ 1/10),
- common ($\geq$ 1/100, <1/10),
- uncommon ($\geq$ 1/1000, <1/100),
- rare ($\geq$ 1/10000, <1/1000),
- very rare (<1/10000),
- not known (cannot be estimated from the available data).

MedDRA System organ class	Frequency	Undesirable Effects
Infections and infestations	Uncommon	Fungal infection including Candida infection, Pathogen resistance
Blood and lymphatic system disorders	Uncommon	Leukopenia, Eosinophilia
	Rare	Thrombocytopenia, Neutropenia
	Not known	Pancytopenia, Agranulocytosis, Haemolytic anaemia
Immune system disorders	Rare	Angioedema, Hypersensitivity
	Not known	Anaphylactic shocka, Anaphylactoid shocka

Metabolism and nutritional disorders	Uncommon	Anorexia
	Rare	Hypoglycaemia particularly in diabetic patients
	Not known	Hyperglycaemia, Hypoglycaemic coma
Psychiatric disorders*	Common	Insomnia
	Uncommon	Anxiety, Confusional state, Nervousness
	Rare	Psychotic reactions (with e.g. hallucination, paranoia), Depression, Agitation, Abnormal dreams, Nightmares
	Not known	Psychotic disorders with self-endangering behaviour including suicidal ideation or suicide attempt
Nervous system disorders*	Common	Headache, Dizziness
	Uncommon	Somnolence, Tremor, Dysgeusia
	Rare	Convulsion, Paraesthesia
	Not known	Peripheral sensory neuropathy, Peripheral sensory motor neuropathy, Parosmia including anosmia, Dyskinesia, Extrapyramidal disorder, Ageusia, Syncope, Benign intracranial hypertension
Eye disorders*	Rare	Visual disturbances such as blurred vision
	Not known	Transient vision loss
Ear and Labyrinth disorders*	Uncommon	Vertigo
	Rare	Tinnitus
	Not known	Hearing loss, Hearing impaired
Cardiac disorders**	Rare	Tachycardia, Palpitation
	Not known	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
Vascular disorders**	Common	Phlebitis
	Rare	Hypotension
Respiratory, thoracic and mediastinal disorders	Uncommon	Dyspnoea
	Not known	Bronchospasm, Pneumonitis allergic
Gastrointestinal disorders	Common	Diarrhoea, Vomiting, Nausea
	Uncommon	Abdominal pain, Dyspepsia, Flatulence, Constipation
	Not known	Diarrhoea–haemorrhagic which in very rare cases may be indicative of enterocolitis, including pseudomembranous colitis, Pancreatitis
Hepatobiliary disorders	Common	Hepatic enzyme increased (ALT/AST, alkaline phosphatase, GGT)
	Uncommon	Blood bilirubin increased
	Not known	Jaundice and severe liver injury, including fatal cases with acute liver failure, primarily in patients with severe underlying diseases, Hepatitis
Skin and subcutaneous tissue disordersb	Uncommon	Rash, Pruritus, Urticaria, Hyperhidrosis
	Not known	Toxic epidermal necrolysis, Stevens-Johnson syndrome, Erythema multiforme, Photosensitivity reaction, Leukocytoclastic vasculitis, Stomatitis
	Rare	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), Fixed drug eruption
Musculo-skeletal and connective tissue disorders*	Uncommon	Arthralgia, Myalgia
	Rare	Tendon disorder including tendinitis (e.g. Achilles tendon), Muscular weakness which may be of special importance in patients with myasthenia gravis
	Not known	Rhabdomyolysis, Tendon rupture (e.g. Achilles tendon), Ligament rupture, Muscle rupture, Arthritis
Renal and urinary disorders	Uncommon	Blood creatinine increased
	Rare	Renal failure acute (e.g. due to interstitial nephritis)
General disorders and administration site conditions*	Common	Infusion site reaction (pain, reddening)
	Uncommon	Asthenia
	Rare	Pyrexia
	Not known	Pain (including pain in back, chest, and extremities)
Endocrine disorders	Rare	Syndrome of inappropriate secretion of antidiuretic hormone (SIADH)

- *[a]Anaphylactic and anaphylactoid reactions may sometimes occur even after the first dose.*
- *[b]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.*
- ***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.*

Other undesirable effects which have been associated with fluoroquinolone administration include:

- *• attacks of porphyria in patients with porphyria.*

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Kindly report any suspected adverse reactions to pharmavigil@jbcpl.com

OVERDOSE

According to toxicity studies in animals or clinical pharmacology studies performed with supra-therapeutic doses, the most important signs to be expected following acute overdose of levofloxacin are CNS symptoms such as confusion, dizziness, impairment of consciousness, and convulsive seizures, increases in QT interval.

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. Haemodialysis, including peritoneal dialysis and CAPD, are not effective in removing levofloxacin from the body. No specific antidote exists.

PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Quinolone antibacterials, Fluoroquinolones.

Pharmacodynamic Properties

Levofloxacin is a synthetic antibacterial agent of the fluoroquinolone class and is the S (-) enantiomer of the racemic drug substance ofloxacin. As a fluoroquinolone antibacterial agent, levofloxacin acts on the DNA-DNA-gyrase complex and topoisomerase IV. Levofloxacin inhibits bacterial type II topoisomerases, topoisomerase IV and DNA gyrase. Levofloxacin, like other fluoroquinolones, inhibits the A subunits of DNA gyrase, two subunits encoded by the gyrA gene. This results in strand breakage on a bacterial chromosome, supercoiling, and resealing; DNA replication and transcription is inhibited.

Pharmacokinetic Properties

Orally administered levofloxacin is rapidly and almost completely absorbed with peak plasma concentrations being obtained within 1h. The absolute bioavailability is approximately 100%. Food has little effect on the absorption of levofloxacin. Approximately 30 - 40% of levofloxacin is bound to serum protein. 500mg once daily multiple dosing with levofloxacin showed negligible accumulation. There is modest but predictable accumulation of levofloxacin after doses of 500mg twice daily. Steady-state is achieved within 3 days.

Levofloxacin is metabolised 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. Levofloxacin is stereochemically stable and does not undergo chiral inversion.Following oral and intravenous administration of levofloxacin, it is eliminated relatively slowly from the plasma ($t_{½}$: 6 - 8 h). Excretion is primarily by the renal route (> 85% of the administered dose). There are no major differences in the pharmacokinetics of levofloxacin following intravenous and oral administration, suggesting that the oral and intravenous routes are interchangeable.

INCOMPATIBILITY

This medicinal product must not be mixed with heparin or alkaline solutions (e.g. sodium hydrogen carbonate) and not be mixed with other medicinal products.

Mixture with other solutions for infusion: Levofloxacin 5mg/ml Solution for Infusion is compatible with the following solutions for infusion: Sodium chloride 9 mg/ml (0.9%) solution, Dextrose 50 mg/ml (5%) injection, Dextrose 50 mg/ml (5%) in lactated Ringer's solution, Dextrose 25 mg/ml (2.5%) in Ringer's solution, Combination solutions for parenteral nutrition (amino acids, carbohydrates, electrolytes).

The solution should be visually inspected prior to use. It must only be used if the solution practically free from particles.

In use: From a microbiological point of view, the product should be used immediately. If not used immediately (within 3 hours), in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Chemical and physical in use stability has been demonstrated for 72 hours at 25°C in 0.9% sodium chloride solution, 5% dextrose solution and 5% dextrose in lactated Ringer's solution, and 24 hours at 2-8°C in combined solutions for parenteral nutrition.

DESCRIPTION

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

STORAGE INSTRUCTIONS

Store below 30°C. Protect from light & moisture. Do not freeze.

Keep medicine out of reach of children.

PACKAGING INFORMATION

Levofloxacin Infusion is available in 100 ml bottle.

Marketed by & ® Regd. Trade Mark of :
J. B. CHEMICALS & PHARMACEUTICALS LTD.
Neelam Centre, 'B' Wing, Hind Cycle Road,
Worli, Mumbai - 400 030. India.

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Note: This prescribing information is applicable for India Market only.