Indications	Daily Dose (mg)	Duration (Days)
Community acquired pneumonia and nosocomial pneumonia	250mg bid or 500mg od	7-14
	750mg od	5
Typhoid fever paratyphoid fever	250mg bid or 500mg od	10-14
Uncomplicated skin and soft tissue infections	250mg bid or 500mg od	7-10
Uncomplicated urinary tract infections	250mg od	3
Complicated urinary tract infections	250mg od	10
Acute pyelonephritis	250mg od	10

Note: Dosage may be adjusted according to the kind of infection and severity of the symptoms.

Dosage in patients with impaired ranal function (creatinine clearance ≤50 ml/min).

Creatinine Clearance	Dose Regimen	
	Initial dose 250mg / 24 hrs.	Initial dose 500mg / 24 hrs.
50 - 20 ml/min	No adjustment required	250mg / 24 hrs
19 - 10 ml/min	250mg / 48 hrs.	250mg / 48 hrs.
Hemodialysis and CAPD	250mg / 48 hrs.	250mg / 48 hrs.

Note: No additional doses are required after hemodialysis or continuous ambulatory peritoneal dialysis (CAPD).

ADVERSE REACTIONS:
Levofloxacin is usually well tolerated. However, following are the adverse effects reported during its therapy.
General: Allergic reactions (anaphylactic/anaphylactoid reaction) with symptoms such as urticaria, cramping of bronchi and possibly severe breathing problems, as well as in very rare cases swelling of the skin and mucous membranes.
Skin reactions and general skin reaction: Itching and rash.
Gastrointestinal tract/metabolism: Nausea and diarrhoea, loss of appetite, vomiting, pain in the abdomen region, dyspepsia, bloody diarrhoea that in very rare cases may be indicative of enterocolitis, including pseudomembranous colitis.
Nervous system: Headache, vertigo / dizziness, drowsiness, sleeping problems, paraesthesia e.g. like tingling in the hands, trembling, restlessness, anxiety, convulsions and confusions.
Cardiovascular system: Abnormally rapid beating of the heart, drop of blood pressure and circulatory (shock like) collapse.
Effects on muscles, tendon and bones: Tendon pain including inflammation, joint pain or muscle pain. Tendon rupture (Achilles Tendon), this side effect may occur within 48 hours after starting treatment and may be bilateral muscular weakness, which may be of special importance in patients with myasthesia gravis (a rare disease of nervous systems).
Liver and kidney: Increased levels of liver enzymes (e.g. ALT, AST) increased level of bilirubin and serum creatinine, inflammation of the liver, disturbance of kidney function up to kidney failure.
Effect on the blood: Increase of certain blood cells (eosinophillia) decrease in the number of white blood cells (leukopenia).

CONTRAINDICATIONS:
Levofloxacin is contraindicated in patients with a history of hypersensitivity to this drug and/or other quinolones. Levofloxacin is contraindicated in children and adolescents as cartilage damages cannot be excluded.

DRUG INTERACTIONS:
Antacids, Sucralfate, Metal Cations, Multivitamins: Concurrent administration of levofloxacin with antacids containing magnesium or aluminum as well as sucralfate, metal cations such as iron and multivitamin preparations with zinc 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 administration.
Theophylline, Warfarin, Cyclosporine, Digoxin, Probenecid and Cimetidine: No Significant effect of levofloxacin on the plasma concentrations, and other disposition parameters for theophylline, warfarin, cyclosporine, digoxin, probenecid and cimetidine was detected in a clinical study.
Non-steroidal anti-inflammatory drugs: 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.
Antidiabetic agents: Disturbances of blood glucose, including hyperglycemia and hypoglycemia, have been reported in patients treated concomitantly with quinolones and an antidiabetic agent (e.g. glyburidelglibenclamide) or insulin. Therefore, careful monitoring of blood glucose is recommended when these agents are co-administered.

OVERDOSAGE:
Levofloxacin exhibits a low potential for acute toxicity. In the event of an acute overdosage, the stomach should be emptied. The patient should be observed and appropriate hydration maintained. Levofloxacin is not efficiently removed by hemodialysis or peritoneal dialysis.

HOW SUPPLIED:
LOCUS 250mg tablets are available in Alu Alu pack of 10 tablets.
LOCUS 500mg tablets are available in Alu Alu pack of 10 tablets.
LOCUS 500mg infusion is available in 100ml vial.

STORAGE:
For Tablets: Store at or below 25°C.
To be sold on the prescription of a registered medical practitioner only.
For Infusion: Store between 15°C to 30°C.
Protect from freezing & sunlight.
Keep out of the reach of children.

ہدایات: ٹیبلٹس کیلئے: دوا کو 25°C پر یا اس سے کم درجہ حرارت پر رکھیں۔
تمام ادویات بچوں کی پہنچ سے دُور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کریں۔
انفیوژن کیلئے: دوا کو 15°C سے 30°C درجہ حرارت کے درمیان رکھیں۔
منجمد ہونے اور دھوپ سے بچائیں۔
بوتل لیک ہو یا اس میں کوئی شے نظر آئے
تو ہرگز استعمال نہ کریں۔

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RAM/11/07

Locus

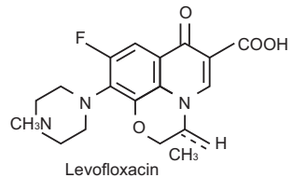
Tablets 250mg 500mg
Infusion 500mg

(Levofloxacin U.S.P)

لوکس ٹیبلٹس ۲۵۰ ملی گرام ۵۰۰ ملی گرام
انفیوژن ۵۰۰ ملی گرام

(لیوفلاکساسین یو۔ایس۔پی)

Composition for tablet:
Each film coated tablet contains Levofloxacin U.S.P.....250mg
Each film coated tablet contains Levofloxacin U.S.P.....500mg
Product complies with U.S.P Specs.
Composition for infusion:
Each 100ml vial contains Levofloxacin as hemihydrate U.S.P 500mg.
Product complies with Saffron specs.



Levofloxacin

DESCRIPTION:
LOCUS (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 C18H20FN3O4 and the structural formula is:

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 DNA gyrase (topoisomerase), which is essential in the reproduction of bacterial DNA.
Levofloxacin has in-vitro activity against the gram-negative and gram-positive microorganisms. It is often bactericidal at concentrations equal to or slightly greater than inhibitory concentration.

PHARMACOKINETICS:
Absorption: Following a single intravenous dose of levofloxacin, the mean ± SD peak plasma concentration attained was 6.2 ± 1 mg/ml after 500mg dose infused over 60 minutes. Levofloxacin pharmacokinetics is linear and predictable after single or multiple dosing regimens. Steady state conditions are reached within 48 hours following a 500mg once daily dosage regimen. 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 ± 0.2 g/ml after the 500mg doses.
The plasma concentration profile of levofloxacin after i.v. administration is similar and comparable in extent of exposure to that observed for levofloxacin tablets when equal doses are administered. Therefore oral and i.v. routs of administration can be considered interchangeable. Peak plasma concentrations are attained 1-2 hours after oral dosing. Oral administration of levofloxacin with food slightly prolongs the time to peak plasma concentration by approximately 1 hour and slightly decreases the peak plasma concentration by approximately 14%. Therefore levofloxacin can be administered without regard to food.
Distribution: The mean volume of distribution generally ranges from 74-112 litres after single and multiple dosing of 500mg or 750mg doses. 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. Following oral administration, approximately 87% of an administered dose was recovered as unchanged drug in urine within 48 hours, whereas less than 4% of the dose was recovered in feces in 72 hours. 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. These metabolites have little relevant pharmacological activity. 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 approximately 144-226ml/min and 96-142ml/min respectively.
Renal insufficiency: Clearance of levofloxacin is substantially reduced and plasma elimination half-life is substantially prolonged in patients with impaired renal function (creatinine clearance <50ml/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.
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.
Elderly: No significant differences in levofloxacin pharmacokinetics between young and elderly subjects when the subject's differences in creatinine clearance are taken into consideration. Levofloxacin dose adjustment based on age alone is not necessary.

THERAPEUTIC INDICATIONS:
LOCUS (Levofloxacin) is indicated for the treatment of adults (•18 years of age) with mild, moderate, and severe infections caused by susceptible strains of the designated microorganisms in the conditions listed below:
- Acute maxillary sinusitis
- Acute bacterial exacerbation of chronic bronchitis
- Community-acquired pneumonia and nosocomial pneumonia
- Typhoid & paratyphoid fever
- Complicated skin and skin structure infections
- Uncomplicated skin and skin structure infections (mild to moderate) including abscesses, cellulitis, furuncles, impetigo, pyoderma, wound infections
- Complicated urinary tract infections (mild to moderate)

Uncomplicated urinary tract infections (mild to moderate) and acute pyelonephritis (mild to moderate)

DOSAGE AND ADMINISTRATION:
Tablets: LOCUS (Levofloxacin) are administered once or twice daily. The dosage depends on the types and severity of the infections and the sensitivity of the presumed, causative pathogen. LOCUS (Levofloxacin) should be swallowed without crushing and with sufficient amount of liquid. The tablets may be taken during meals or between meals. LOCUS (Levofloxacin) tablets should be administered at least two hours before or two hours after antacids containing magnesium, aluminium, as well as sucralfate, metal cations such as iron and multivitamin preparations with zinc.
Infusion: Rapid or bolus intravenous infusion must be avoided. Infusion time should not be less than 60 minutes, depending on the dosage. The usual dose of Locus (levofloxacin) I.V. infusion in 250mg or 500mg over 60 minutes administered once or twice daily. The dosage depends on the types and severity of infections and the sensitivity of the presumed, causative pathogen.

The dosage guidelines as per the infection are given as under.

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

Indications	Daily Dose (mg)	Duration (Days)
Acute maxillary sinusitis	250mg bid or 500mg od	10-14
Acute bacterial exacerbation of chronic bronchitis	250mg bid or 500mg od	7