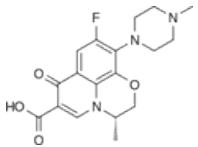
S-flox® 250mg 500mg

ایس۔فلوکس

(L e v o f l o x a c i n)
Tablets USP

DESCRIPTION:
S-FLOX (Levofloxacin) is a synthetic broad-spectrum antibacterial agent. The molecular formula of levofloxacin is C_{18} H_{20} FN_3O_4 and the structural formula is:



QUALITATIVE AND QUANTITATIVE COMPOSITION:
S-FLOX Tablets USP 250mg
Each film-coated tablet contains:
Levofloxacin Hemihydrate eq.
to Levofloxacin USP.....250mg

S-FLOX Tablets USP 500mg
Each film-coated tablet contains:
Levofloxacin Hemihydrate eq.
to Levofloxacin USP 500mg

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

PHARMACOKINETICS:
Absorption
Levofloxacin is rapidly and essentially completely absorbed after oral administration. Peak plasma concentrations are attained 1-2 hours after oral dosing. The absolute bioavailability is approximately 99% demonstrating complete oral absorption of levofloxacin. Levofloxacin pharmacokinetics are linear and predictable after single and multiple dosing regimens. Steady state conditions are reached within 48 hours following a 500mg or 750 mg once daily dosage regimens. The mean ±SD peak and trough plasma concentrations attained following multiple once-daily oral dosage regimens were approximately 5.7±1.4 and 0.5±0.2µg/ml after the 500mg doses, and 8.6±1.9 and 1.1±0.4µg/ml after the 750mg doses, respectively. Oral administration of a levofloxacin with food slightly prolongs the time to peak concentration by approximately 1 hour and slightly decreases the peak concentration by approximately 14%. Therefore levofloxacin can be administered without regard to food.

Distribution
The mean volume of distribution generally ranges from 74 – 112 liters 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 human is primarily excreted as unchanged drug in the urine. Following oral administration approximately 87% of and 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 indentified 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 approx. 144-226ml/min and 96-142,ml/min respectively.

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.

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

INDICATIONS	DAILY DOSE (mg)	DURATION (DAYS)
Acute Bacterial Sinusitis	500mg od	10 – 14
Acute Bacterial Exacerbation of Chronic Bronchitis	250mg bid or 500mg od	7
Community Acquired Pneumonia and	250mg bid or 500mg od	7 – 14
Nosocomial Pneumonia	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
Complicated Skin and Soft Tissue Infections	750mg od	7 – 14
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 renal function (creatinine clearance < 50ml/min)

Creatinine Clearance	Dose regimen		
	Initial dose 250mg/24hr	Initial dose 500mg/24hr.	Initial dose 750mg/24hr.
50-20 ml/min	No adjustment Required	250mg/24hr.	750mg/48hr.
19 - 10 ml/min	250mg/48hr.	250mg/48hr.	500mg/48hr.
hemodialysis & CAPD	250mg/48hr.	250mg/48hr.	500mg/48hr.

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/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 membrane.

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 diarrohea 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, inflamation 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.

Renal insufficiency
Levofloxacin should be administered with caution in the presence of renal insufficiency. In patients with impaired renal function (creatinine clearance <50ml/min) adjustment of the dose regimen is necessary to avoid the accumulation of levofloxacin due to decreased clearance.

Pediatric use
Safety and effectiveness of levofloxacin in individuals below 18 years of age have not been established.

Pregnancy
There are no adequate and well-controlled studies in pregnant women. Levofloxacin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
Levofloxacin has not been measured in human milk. Based upon data from ofloxacin, it can be presumed that levofloxacin will be excreted in human milk. Because of the potential for serious adverse reactions from levofloxacin in nursing infants, nursing should not be undertaken by mothers who must use levofloxacin.

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 absorptoin 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, AUC, and other disposition parameters for theophylline, Warfarin, cyclosporine, digoxin, probenecid and cimetidine was detected in a clinical study.

Non-steroidal anti-inflammatory drugs: The concornitant 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.,glyburide/glibenclamide) 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.

STORAGE:
Store below 30°C.
Protect from heat, light & moisture.
Keep all medicines out of the reach of children.

PRESENTATION:
S-FLOX (Levofloxacin) Tablets USP 250mg are available in Alu/Alu blister pack of 1x10's.
S-FLOX (Levofloxacin) Tablets USP 500mg are available in Alu/Alu blister pack of 1x10's.

خوراک : ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں، روشنی، گرمی اور نمی سے محفوظ رکھیں۔
تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

For detailed information please contact:
GENIX
GENIX PHARMA PRIVATE LIMITED
44,45-B, Korangi Creek Road, Karachi-75190, Pakistan.
UAN: +92-21-111-10-10-11, Fax: +92-21-111-10-10-22
E-mail: info@genixpharma.com Web.: www.genixpharma.com

OHSAS 18001
ISO 14001
ISO 9001
122-318-01