STANFLOX
(Levofloxacin) USP

TABLETS
INFUSION

DESCRIPTION

STANFLOX is a synthetic broad spectrum antibacterial fluoroquinolone containing levofloxacin hemihydrate , which is the (-)- S (-).enantiomer (levorotatory form) of the racemic drug substance ofloxacin for oral and intravenous administration with a chemical name of (-)-(s)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1 piperazinyl)-7-oxo-7-H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid hemihydrate. Its empirical formula is $C_{18}H_{20}FN_3O_4 \cdot \frac{1}{2} H_2O$

COMPOSITION

1. STANFLOX Tablet 250mg

Each tablet contains:

Levofloxacin (as hemihydrate) USP.....250mg

2. STANFLOX Tablet 500mg

Each tablet contains:

Levofloxacin (as hemihydrate) USP..... 500mg

3. STANFLOX Infusion 500mg

Each 100ml Infusion 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 the following gram-negative and gram-positive microorganisms. It is often bactericidal at concentrations equal to or slightly greater than inhibitory concentration.

Note: Penicillin resistant S.pneumonia are those strains with a penicillin MIC Value of ≥ug/ml.

AEROBIC GRAM-POSITIVE MICROORGANISMS

- Enterococcus faecalis (many strains are only moderately susceptible)
- Staphylococcus aureus (methicillin-susceptible strains)
- Staphylococcus epidermidis (methicillin-susceptible strains)
- Staphylococcus saprophyticus
- Streptococcus pneumoniae (including Penicillin resistant strains)
- Streptococcus Pyogens

AEROBIC GRAM-NEGATIVE MICROORGANISMS

- Enterobacter cloacae
- Escherichia coli
- Haemophilus influenzae
- 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.

OTHER MICROORGANISMS

- CHLAMYDIA PNEUMONIAE
- MYCOPLASMA PNEUMONIAE

In vitro there is cross-resistance between STANFLOX and other fluoroquinolones.

PHARMACOKINETICS

ABSORPTION

Following a single intravenous dose of levofloxacin, the mean ± SD peak plasma concentration attained was 6.2 ± 1.0 ug/ml after a 500mg dose infused over 60 minutes.

Levofloxacin pharmacokinetics are linear and predictable after single and multiple dosing regimens. Steady-state conditions are reached within 48 hours following a 500mg or 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 ± 0.2 ug/ml after the 500mg doses.

DISTRIBUTION

Levofloxacin is approximately 24 to 38% bound to serum proteins Levofloxacin is mainly bound to serum albumin in humans. Levofloxacin binding 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.

These metabolites have little relevant pharmacological activity. The mean terminal plasma elimination half-life of levofloxacin ranges from approximately 6 to 8 hours following single or multiple doses of levofloxacin.

SPECIAL POPULATIONS

RENAL INSUFFICIENCY: Clearance of levofloxacin is substantially reduced and plasma elimination half-life is substantially prolonged in 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.

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.

GERIATRIC: There are no significant differences in levofloxacin pharmacokinetics between young and elderly subjects. Levofloxacin dose adjustment based on age alone is not necessary.

PEDIATRIC: The pharmacokinetics of levofloxacin in pediatric subjects have not been studied.

GENDER: There are no significant differences in levofloxacin pharmacokinetics between male and female subjects. Dose adjustment based on gender alone is not necessary.

THERAPEUTIC INDICATIONS

STANFLOX injections are 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, STANFLOX Injection is indicated when intravenous administration offers a route of administration advantageous to the patient:

- Acute maxillary sinusitis
- Acute bacterial exacerbation of chronic bronchitis
- Community-acquired pneumonia & Nosocomial pneumonia
- 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)
- Acute pyelonephritis (mild to moderate)

DOSAGE AND ADMINISTRATION

STANFLOX INFUSION

STANFLOX Injection should only be administered by intravenous infusion. It is not for intramuscular, intrathecal, intraperitoneal, or subcutaneous administration. **RAPID OR BOLUS INTRAVENOUS INFUSION MUST BE AVOIDED**. Levofloxacin Injection should be infused intravenously slowly over a period of not less than 60 or 90 minutes, depending on the dosage. The usual dose of STANFLOX Injection is 250mg or 500mg administered by slow infusion over 60 minutes every 24 hours. The dose depends on the types and severity of the infections and the sensitivity of the presumed, causative pathogen.

STANFLOX TABLETS

STANFLOX (Levofloxacin) tablets 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, STANFLOX (levofloxacin) tablets should be swallowed without crushing and with sufficient amount of liquid. The tablets may be taken during meals or between meals. STANFLOX (Levofloxacin) tablets should be administered at least two hours before or two hours after antacids containing magnesium, aluminum, as well as sucralfate, metal cations such as iron and multivitamin preparations with zinc.

The dosage guidelines as per the infusion and tablets are given as under.

DOSAGE IN PATIENTS WITH NORMAL RENAL FUNCTION (CREATININE CLEARANCE > 5Oml/min)

INDICATIONS	DAILY DOSE (mg)	DURATION (DAYS)
Acute Maxillary Sinusitis	250mg bid or 500mg od	10-14
Acute Bacterial Exacerbation or Chronic Bronchitis	250mg bid or 500mg od	7
Community Acquired Peumonia and Nosocomial Pneumonia	250mg bid or 500mg od / 750mg od	7-14/5
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

DOSAGE IN PATIENTS WITH IMPAIRED RENAL FUNCTION (CREATININE CLEARANCE > 50ml/min)

DOSAGE IN NORMAL RENAL FUNCTIONS EVERY 24 HOURS	CREATININE CLEARANCE 20 TO 49ml/min	CREATININE CLEARANCE 10 TO 19ml/min	HEMODIALYSIS OR CHRONIC AMBULATORY PERITONEAL DIALYSIS (CAPD)
750mg	750mg every 48 hours	750mg initial dose, then 500mg every 48 hours	750mg initial dose, then 500mg every 48 hours
500mg	500mg initial dose, then 250mg every 24 hours	500mg initial dose, then 250mg every 48 hours	500mg initial dose, then 250mg every 48 hours
250mg	No dosage adjustment	250mg every 48 hours. If treating uncomplicated UTI, then no dosage adjustment is required	No information on dosing adjustment is available

ADVERSE REACTIONS

STANFLOX (Levofloxacin) is usually well tolerated. However, in general 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.

GASTRO-INTESTINAL TRACT/METABOLISM: nausea and diarrhea, loss of appetite, vomiting, pain in the abdomen region, dyspepsia, bloody diarrhea that in very rare cases may be indicative of enterocolitis, including pseudomembranous colitis.

NERVOUS SYSTEM: Headache, vertigo/dizziness, drowsiness, sleeping problems, parasthesia, 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 the kidney function up to kidney failure.

EFFECT ON THE BLOOD: Increase of certain blood cells (eosinophillia) decrease in the number of white blood cells (leucopenia).

CONTRAINDICATIONS

Levofloxacin is contraindicated in persons with a history of hypersensitivity to levofloxacin, quinolone antimicrobial agents, or any other components of this product.

Levofloxacin is contraindicated in children and adolescents as cartilage damage cannot be excluded.

PRECAUTIONS

GENERAL

- Because a rapid or bolus intravenous injection may result in hypotension, LEVOFLOXACIN INJECTION SHOULD ONLY BE ADMINISTERED BY SLOW INTRAVENOUS INFUSION OVER A PERIOD OF 60 OR 90 MINUTES DEPENDING ON THE DOSAGE.
- Although levofloxacin is more soluble than other quinolones, adequate hydration of patients receiving levofloxacin should be maintained to prevent the formation of a highly concentrated urine.
- Moderate to severe phototoxicity reactions have been observed in patients exposed to direct sunlight while receiving drugs in this class. Excessive exposure to sunlight should be avoided. Therapy should be discontinued if phototoxicty (e.g., a skin eruption) occurs.
- As with other quinolones, levofloxacin should be used with caution in any patient with a known or suspected CNS disorder that may predispose to seizures or lower the seizure threshold.
- Serious and occasionally fatal hypersensitivity and/or anaphylactic reactions have been reported in patients receiving therapy with quinolones including levofloxacin. These reactions often occur following the first dose. Levofloxacin should be discontinued immediately at the first appearance of a skin rash or any other sign of hypersensitivity.
- Levofloxacin should be discontinued if the patient experiences pain, inflammation, or rupture of a tendon during therapy.
- As with any potent antimicrobial drug, periodic assessment of organ system functions, including renal, hepatic, and hematopoietic, is advisable during therapy.

RENAL INSUFFICIENCY

Administer levofloxacin with caution in the presence of renal insufficiency. Careful clinical observation and appropriate laboratory studies should be performed prior to and during therapy, since elimination of levofloxacin may be reduced. In patients with impaired renal function (creatinine clearance <50 ml/min), adjustment of the dosage 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

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, 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.

DRUG INTERACTIONS

ANTIDIABETIC AGENTS: Disturbances of blood glucose, including hyperglycemia and hypoglycemia, have been reported in patients treated concomitantly with quinolones and an anti-diabetic agent. Therefore, careful monitoring of blood glucose is recommended when these agents are co-administered.

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.

MULTIVALENT CATIONS: No quinolone should be co-administered with any solution containing multivalent cations, e.g., magnesium, through the same intravenous line.

OVER-DOSAGE

STANFLOX (Levofloxacin) exhibits a low potential for acute toxicity. In the event of an acute over-dosage, the stomach should be emptied. The patient should be observed and appropriate hydration maintained. Levofloxacin is not efficiently removed by hemodialysis or peritoneal dialysis.

INSTRUCTIONS

FOR TABLETS

Store below 30°C. Protect from heat, light & moisture.

FOR INFUSION

Store below 30°C. Do not refrigerate. Protect from heat & light. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

Keep in the pack until required. Once the infusion vial has been opened, the infusion solution must be used within three hours.

Note: Do not use if vial is leaking, solution is cloudy or contains undissolved particles. To be administered by slow I.V. Infusion over a period of 60 minutes.

PRESENTATION

TABLETS

STANFLOX (Levofloxacin) Tablets 250mg & 500mg are available in Alu-Alu pack of 2x5 tablets.

INFUSION

STANFLOX (Levofloxacin) 500mg: 1 vial of 100ml solution for I.V. Infusion per carton.

سٹینفلوکس ٹیبلیٹس/انفیوژن
(لیوو فلوکساسین) یو ایس پی

ہدایات:

برائے ٹیبلیٹس

30° سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے محفوظ رکھیں۔

برائے آئی وی انفیوژن

دوا کو 30° سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ منجمد ہونے سے بچائیں۔ گرمی اور روشنی سے بچائیں۔ تمام دوائیں بچوں کی پہنچ سے دُور رکھیں۔ صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔ جب تک ضرورت نہ ہو دوا کو ڈبے کے اندر رکھیں۔ وائل کھولنے کے بعد دوا کو تین گھنٹے کے اندر استعمال کریں۔

نوٹ: وائل کے لیک ہونے، دھندلا ہونے یا اس میں غیر حل پذیر ذرات نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔ آئی وی انفیوژن مریض کے جسم میں 60 منٹ کے دوران داخل کیا جائے۔

Manufactured by:
STANDPHARM PAKISTAN (PVT) LTD
20 km Ferozepur Road Lahore, Pakistan.