LEVOFLOXACIN

CEFLOX 500

500 mg Tablet

Antibacterial

℞

FORMULATION:
Each tablet contains:
Levofloxacin, USP ..... 500 mg

DESCRIPTION:
Light green, oval, biconvex, film-coated tablet, bisected on one side.

PHARMACODYNAMICS AND PHARMACOKINETICS:
Levofloxacin is a synthetic broad-spectrum fluoroquinolone. It is generally considered to be about twice as active as its isomer, ofloxacin. Levofloxacin has a broad spectrum of activity which includes both gram-positive and gram-negative bacteria. Levofloxacin inhibits bacterial DNA synthesis by blocking the activities of bacterial topoisomerase type II (DNA gyrase) and topoisomerase IV. These enzymes are required for replication and transcription of bacterial DNA. Inhibition of the DNA gyrase prevents formation of supercoiled DNA resulting in bacterial cell death that is required for normal transcription and replication. Inhibition of topoisomerase IV interferes with separation of replicated chromosomal DNA into respective daughter cells during cell division.

Levofloxacin is active against a wide spectrum of gram-positive and gram-negative microorganisms. Some microorganisms resistant to other fluoroquinolones maybe susceptible to levofloxacin. Levofloxacin has a superior activity against gram-positive microorganisms including *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Staphylococcus epidermidis*. Levofloxacin is indicated for the treatment of bacterial infections of the respiratory tract, urinary tract, gastrointestinal tract, central nervous system, and infections in immunocompromised patients caused by: *Enterobacteriaceae*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Staphylococcus aureus*, *Haemophilus parainfluenzae*, *Pseudomonas aeruginosa*, *Serratia marcescens*, *Escherichia coli*, *Klebsiella pneumonia*, *Proteus*, *Providencia*, *Salmonella*, *Serratia*, *Shigella and Yersinia spp*. It may also exhibit activity against *Pseudomonas aeruginosa*, *Neisseria gonorrhea*, and *Chlamydia trachomatis*

After oral intake, Levofloxacin is rapidly and completely absorbed with peak plasma concentration of about 1-2 hours. Levofloxacin has relatively poor penetration into the cerebrospinal fluid, but is widely distributed into the body tissues including the bronchial mucosa. Levofloxacin has an elimination half-life of about 6-8 hours. Half-life may be extended in patient with renal impairment. Excretion is primarily in the urine with less than 5% as metabolites. It is excreted largely unchanged. Levofloxacin is not removed by hemodialysis or peritoneal dialysis.

INDICATIONS:
For the treatment of mild, moderate, and severe infections in adults above 18 years old caused by susceptible strains of microorganisms including bacterial conjunctivitis, acute bacterial sinusitis, acute exacerbation of chronic bronchitis, nosocomial pneumonia, community acquired pneumonia, skin infections, wound infections, chronic bacterial prostatitis, uncomplicated and complicated urinary tract infections, and acute pyelonephritis.

DOSAGE AND ADMINISTRATION:
Adults: 250 – 500 mg once or twice daily.
Dose is adjusted in patients with renal impairment.

The dose and duration of treatment is based on the type and severity of the infection:

	DOSE	DURATION OF TREATMENT
Community acquired pneumonia	500 mg 750 mg	7-14 days 5 days
Nosocomial pneumonia	750 mg	7-14 days
Acute bacterial exacerbation of chronic bronchitis	500 mg	7 days
Acute bacterial sinusitis	750 mg	5 days
Complicated skin and skin structure infections	750 mg	7-14 days
Uncomplicated skin and skin structure infections	500 mg	7-10 days
Chronic bacterial prostatitis	500 mg	28 days
Complicated urinary tract infections	750 mg	5 days
Acute pyelonephritis	750 mg	5 days
Uncomplicated urinary tract infection	250 mg	3 days

Or as prescribed by the physician.

CONTRAINDICATIONS/PRECAUTIONS/WARNINGS:
Levofloxacin is contraindicated in patients with history of hypersensitivity to levofloxacin and in patients with history of tendon disorders related to fluoroquinolone therapy.

Like other quinolones, levofloxacin may cause central nervous system events such as nervousness, agitation, insomnia, anxiety, nightmares, and paranoia. Caution must be exercised in patients with epilepsy or a history of CNS disorder. There is a possible exacerbation of symptoms of myasthenia gravis. Patients with known history of myasthenia gravis should avoid using levofloxacin.

The ability to drive or operate machinery may be impaired by levofloxacin, especially when alcohol is also taken.

Levofloxacin should not be used in children, adolescents, pregnant women or breast-feeding mothers. Tendon damage may occur and treatment should be discontinued in the presence of signs and symptoms of tendon inflammation or rupture. Care is necessary in patients with impaired hepatic or renal function and glucose-6-phosphate dehydrogenase deficiency.

An adequate fluid intake should be maintained during treatment with levofloxacin. Rarely, crystalluria may be observed if the urine has excessive alkalinity.

There have been reports of phototoxicity in some patients who are exposed to direct sunlight while receiving quinolones, manifested as exaggerated sunburn response, thus excessive exposure to sunlight or sunlamps should be avoided. Therapy should be discontinued if phototoxicity occurs. As with any potent drug, assessment of organ system function should be done periodically, particularly if the drug is taken for long periods.

Patients taking hypoglycemic agents or insulin should have their blood-glucose concentrations closely monitored, and if signs and symptoms of glucose disturbances develop, levofloxacin should be stopped.

PREGNANCY AND LACTATION:
Levofloxacin is generally not recommended for use in pregnant or breast-feeding women because of its propensity to cause joint erosions.

ADVERSE DRUG REACTIONS:
Levofloxacin generally has good tolerability. Most adverse effects involve gastrointestinal tract, CNS, and skin. Gastrointestinal disturbances constitute the most common adverse reactions. These include nausea, vomiting, diarrhea, abdominal pain, dyspepsia, and rarely, pseudomembranous colitis, pancreatitis, and dysphagia.

Most common CNS adverse reactions include headache, dizziness, confusion, insomnia, and restlessness. Less commonly, there may be tremors, drowsiness, nightmares, visual and other sensory disturbances, hallucinations, psychotic reactions, depression, convulsions, paresthesia, and peripheral neuropathy.

Skin reactions are of the hypersensitivity type and include rash and pruritus. Rarely, there have been reports of vasculitis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, photosensitivity, and anaphylaxis. Like other quinolones, reversible arthralgia, myalgia, and tendon damage have occured rarely with levofloxacin.

Adverse effects of varying frequencies involving other organ systems have been reported with levofloxacin and includes transient increases in serum creatinine or BUN, acute renal failure, crystalluria, elevated liver enzyme values, jaundice, hepatitis, hemolytic anemia, and agranulocytosis.

Prolonged use of levofloxacin may lead to superinfection by non-susceptible organisms such as Candida, Clostridium difficile, Streptococcus pneumoniae, Staphylococcus aureus and Enterococci.

DRUG INTERACTIONS:
Like other quinolones, levofloxacin must be administered at least 2 hours before or 2 hours after taking antacids containing magnesium and aluminum, sucralfate, or multivitamins with zinc and iron since these agents interfere with the gastrointestinal absorption of levofloxacin. Sucralfate may reduce absorption of levofloxacin.

Daily products with high calcium content may also interfere with the absorption of some fluoroquinolones.

Symptomatic hyperglycemia and/or hypoglycemia have been reported in diabetic patients taking hypoglycemic agents or insulin.

Fluoroquinolones inhibit the cytochrome P450 isoenzyme CYP1A2 and may increase plasma concentrations of drugs such as theophylline and tizanidine that are metabolized by this isoenzyme.

Levofloxacin has been shown to decrease clearance of theophylline. This can lead to elevated plasma concentrations of theophylline and increased risk of theophylline-related adverse effects, including seizures.

Levofloxacin enhances the effects of the oral anticoagulant warfarin and its derivatives.

Levofloxacin may increase the risk of CNS stimulation and convulsive seizures if used concomitantly with non-steroidal anti-inflammatory drugs (NSAIDs).

Levofloxacin may inhibit the metabolism of ciclosporin in renal transplant patients.

Some fluoroquinoles have the potential to prolong the QT interval and should be avoided in patients receiving class Ia antiarrhythmic drugs such as quinidine and procainamide or class III antiarrhythmics such as amiodarone and sotalol.

Caution should be exercised when levofloxacin is used with other drugs such as the antihistamines, astemizole and terfenadine, cisapride, erythromycin, pentamidine, phenothiazines, or tricyclic antidepressants.

OVERDOSE AND TREATMENT:
Acute overdose of levofloxacin may result in gastrointestinal, cardiac, and CNS symptoms that may include an impaired level of consciousness, confusion, dizziness, and seizures.

ECG changes such as prolongation of the QT interval may be noticed. Gastrointestinal reactions like nausea, vomiting, and mucosal erosions may occur.

Treatment for overdose should be symptomatic. Patients should be closely observed and hydrated properly and ECG monitoring is necessary because of the possibility of prolonged QT interval.

Giving activated charcoal as soon as possible after oral overdose may prevent excessive increase of systemic levofloxacin exposure. Antacids may be used for protection of the gastric mucosa.

Hemodialysis, including peritoneal dialysis and continuous ambulatory peritoneal dialysis, are not effective in removing levofloxacin from the body. There is no specific antidote available at present.

AVAILABILITY:
Blister pack x 10's (Box of 30's)

CAUTION:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

DR-XY35957

STORE AT TEMPERATURES NOT EXCEEDING 30°C.

For suspected adverse drug reaction, Report to the FDA:
www.fda.gov.ph

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#16 Scout Tuazon cor. Roces Ave., Quezon City
Metro Manila Philippines
by: **Hizon Laboratories, Inc.**
Assumption Road, Sumulong Highway
Antipolo City

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