CEVAL 250 mg 500 mg Tablet
(ciprofloxacin)

سی وال
(سپروفلاکساسین)

DESCRIPTION
CEVAL (Ciprofloxacin hydrochloride) Tablets is a synthetic broad spectrum antimicrobial agent for oral administration.
Chemically ciprofloxacin hydrochloride, a fluoroquinolone, is the monohydrochloride monohydrate salt of1-cyclopropyl-6-fluoro-1, 4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid.The molecular formula is $C_{17}H_{18}FN_3O_3$-HCl-H_2O and its structural formula is:
COMPOSITION
Each film-coated tablet contains
Active ingredient: Ciprofloxacin HCl USP equivalent to ciprofloxacin …250mg
Each film-coated tablet contains
Active ingredient: Ciprofloxacin HCl USP equivalent to ciprofloxacin …500mg

CLINICAL PHARMACOLOGY
Mechanism of Action
Ciprofloxacin is a synthetic 4-quinolone derivative, with bactericidal activity. It acts via inhibition of bacterial DNA gyrase (topoisomerase, which is essential in the reproduction of bacterial DNA), ultimately resulting in interference with DNA function. Ciprofloxacin is highly active against a wide range of Gram-positive and Gram-negative organisms and has shown activity against some anaerobes.

Microbiology
Ciprofloxacin has in vitro activity against a wide range of gram-negative and gram-positive microorganisms.
Aerobic gram-positive microorganisms
Enterococcus faecalis (Many strains are only moderately susceptible.)
Staphylococcus aureus (methicillin-susceptible strains only)
Staphylococcus epidermidis
Streptococcus pneumoniae, Streptococcus pyogenes

Aerobic gram-negative microorganisms
Campylobacter jejuni
Citrobacter diversus
Citrobacter freundii
Enterobacter cloacae
Escherichia coli
Haemophilus influenzae
Haemophilus parainfluenzae
Klebsiella pneumoniae
Moraxella catarrhalis
Morganella morganii
Neisseria gonorrhoeae
Proteus mirabilis
Proteus vulgaris
Providencia rettgeri
Providencia stuartii
Pseudomonas aeruginosa
Salmonella typhi
Serratia marcescens
Shigella boydii
Shigella dysenteriae
Shigella flexneri
Shigella sonnei
Ciprofloxacin has been shown to be active against Bacillus anthracis both in vitro and by use of serum levels as surrogate marker
Pharmacokinetics
Absorption
When ciprofloxacin is given concomitantly with food, there is a delay in the absorption of thedrug, resulting in peak concentrations that occur closer to 2 hours after dosing rather then 1 hour. The overall absorption of ciprofloxacin is not substantially affected.
Effect of Food
The intake of food at the same time as administration of oral ciprofloxacin has a marginal but clinically not relevant effect on the pharmacokinetic parameters Cmax and AUC. No specific recommendations are necessary with regard to time of administration of oral ciprofloxacin relative to food intake.
Distribution
Plasma protein binding ranges from 20-40%. Ciprofloxacin is widely distributed in the body and tissue penetration is generally good. It appears in the CSF, but concentrations are only about 10% of those in plasma when the meninges are not inflamed. Ciprofloxacin crosses the placenta and is also distributed in to breast milk. High concentrations are achieved in bile.
Metabolism:
Four metabolites have been identified in human urine which together account for approximately 15% of an oral dose. The metabolites have antimicrobial activity, but are less active than unchanged ciprofloxacin. Ciprofloxacin is an inhibitor of human cytochrome P450 1A2 (CYP1A2) mediated metabolism. Coadministration of ciprofloxacin with other drugs primarily metabolized by CYP1A2 results in increased plasma concentrations of these drugs.
Excretion
The serum elimination half-life in subjects with normal renal function is approximately 4 hours. Approximately 40 to 50% of an orally administered dose is excreted in the urine as unchanged drug. The urinary excretion of ciprofloxacin is virtually complete within 24 hours after dosing. The renal clearance of ciprofloxacin, which is approximately 300mL/minute, exceeds the normalglomerular filtration rate of 120mL/minute. Thus, active tubular secretion would seem to play
a significant role in its elimination. Although bile concentrations of ciprofloxacin are several fold higher than serum concentrations after oral dosing, only a small amount of the dose administered is recovered from the bile as unchanged drug. An additional 1 to 2% of the dose is recovered from the bile in the form of metabolites. Approximately 20 to 35% of an oral dosels recovered from the feces within 5 days after dosing. This may arise from either biliary clearance or transintestinal elimination.
Only small amounts of ciprofloxacin are removed by hemodialysis or peritoneal dialysis.
Special Population
Geriatric Patient
Oral plasma concentrations of ciprofloxacin are higher in elderly subjects (> 65 years) as compared to young adults. Although the Cmax is increased 16-40%, the increase in mean AUC is approximately 30%, and can be at least partially attributed to decreased renal clearance in the elderly. Elimination half-life is only slightly (~20%) prolonged in the elderly. These differences are not considered clinically significant.
Renal Insufficiency
In patients with reduced renal function, the half-life of ciprofloxacin is slightly prolonged. Dosage adjustments may be required.
Hepatic Insufficiency
In patients with stable chronic liver cirrhosis, no significant changes in ciprofloxacin pharmacokinetics have been observed.
INDICATIONS
CEVAL (Ciprofloxacin) is indicated for the treatment of the following infections caused by sensitive bacteria:
Adults
Respiratory tract infections: e.g., lobar and bronchopneumonia, acute and chronic bronchitis, acute exacerbation of cystic fibrosis, bronchiectasis, empyema. Ciprofloxacin is not recommendedas first-line therapy for the treatment of pneumococcal pneumonia.
Ciprofloxacin may be used for treating Gram-negative pneumonia.
Ear, nose and throat infections: e.g., mastoiditis, otitis media and sinusitis, especially if due toGram-negative bacteria (including Pseudomonas spp.). Ciprofloxacin is not recommended for the treatment of acute tonsillitis.
Urinary tract infections: e.g., uncomplicated and complicated urethritis, acute uncomplicatedcystitis, pyelonephritis, chronic bacterial prostatitis, epididymitis. Skin and soft tissue infections: e.g., infected ulcers, wound infections, abscesses, cellulitis, otitis externa, erysipelas, infected burns.
Bone and joint infections: e.g., osteomyelitis, septic arthritis.
Complicated intra-abdominal infections: e.g., peritonitis, intra-abdominal abscesses.
Infections of the biliary tract: e.g., cholangitis, cholecystitis, empyema of the gall bladder. Gastro-Intestinal Infections: e.g., enteric fever (typhoid fever), infective diarrhea. Pelvic Infections: e.g., salpingitis, endometritis, pelvic inflammatory disease. Severe systemic infections: e.g., septicaemia, bacteraemia, peritonitis, infections in immunosuppressed patients.
Gonorrhea: including urethral, rectal and pharyngeal gonorrhea caused by -lactamase producing organisms or organisms moderately sensitive to penicillin.
CEVAL (Ciprofloxacin) is also used for the prophylactic treatment against:
1. Infection in elective upper gastro-intestinal tract surgery and endoscopic procedures, where there is an increased risk of infection.
2. Meningococcal meningitis
Children and adolescents
Ciprofloxacin may be used for the 2nd and 3rd line treatment of complicated urinary tract infections and pyelonephritis in children and adolescents 1-17 years of age and for the treatment of acute pulmonary exacerbation of cystic fibrosis associated with P.aruginosa infection in children and adolescents aged 5-17 years of age.
Inhalation Anthrax in Adults and Children
To reduce the incidence or progression of disease following confirmed or suspected exposure to aerosolized Bacillus anthracis.
DOSAGE AND ADMINISTRATION
CEVAL (Ciprofloxacin) tablets can be taken independent of mealtimes. Ciprofloxacin should be administered at least 2 hours before or 6 hours after magnesium/aluminum antacids, or sucralfate, didanosine chewable/buffered tablets or pediatric powder for oral solution, other highly buffered drugs, or other products containing calcium, iron or zinc.
Adults
CEVAL (Ciprofloxacin) tablets should be administered orally to adults as described in the dosage guidelines table. The determination of dosage for any particular patient must take into consideration the severity and nature of the infection, the susceptibility of the causative organism, the integrity of the patient's host-defense mechanisms and the status of renal function and hepatic function.
The dosage range for adults is 100-750mg twice daily. The duration of treatment depends uponthe severity of infection. The usual duration is 7 to 14 days, however, for severe and complicated infections more prolonged therapy may be required.

Indication	Severity	Dosage (mg Ciprofloxacin)	Frequency	Duration of treatment (Days)***
Urinary Tract	Acute uncomplicated mild/moderate Severe/complicated	250mg 250mg 500mg	q 12 hr q 12 hr q 12 hr	3 7 - 14 7 - 14
Chronic bacterial prostatitis	Mild/moderate	500mg	q 12 hr	28
Lower respiratory tract*	Mild/moderate Severe/complicated	500mg 750mg	q 12 hr q 12 hr	7 - 14 7 - 14
Acute Sinusitis	Mild/moderate	500mg	q 12 hr	10
Skin and skin Slurcture	Mild/moderate Severe/complicated	500mg 750mg	q 12 hr q 12 hr	7 - 14 7 - 14
Bone and joint	Mild/moderate Severe/complicated	500mg 750mg	q 12 hr q 12 hr	≥4-6 weeks ≥4-6 weeks
Intra-abdominal**	Complicated	500mg	q 12 hr	7 - 14
Infectious diarrhea	Mild/moderate/ Severe	500mg	q 12 hr	5 - 7
Typhoid fever	Mild/moderate	500mg	q 12 hr	10
Urethral and cervical gonococcal Infections	Uncomplicated	250mg	Single dose	Single dose
Inhalational anthrax (post-exposure)		500mg	q 12 hr	60
Prophylaxis Elective upper gastro-intestinal surgical and endoscopic		750mg single dose 60-90 minutes prior to the procedure		
Meningococcal meningitis		500mg	Single dose	Single dose

*Although the pharmacokinetics of ciprofloxacin remains unchanged in patients with cystic fibrosis, the low body weight of these patients should be taken into consideration when determining dosage.
**Used in conjunction with metronidazole.
***Generally ciprofloxacin should be continued for at least 2 days after the signs and symptoms of infection have disappeared, except for inhalational anthrax (post-exposure).