CEPROXX

Tablets

Composition

Each tablet contains Ciprofloxacin (as Hcl) equivalent to 250 or 500 mg Ciprofloxacin

Action

Ciprofloxacin is a synthetic, fluorinated 4-quinolone antimicrobial agent.
It has broad antimicrobial activity and is effective, after oral administration, for the treatment of a wide variety of infectious diseases. The bactericidal action of Ciprofloxacin results from interference with the enzyme DNA gyrase, needed for the synthesis of bacterial DNA.

Gram-positive aerobes

Corynebacterium species

Staphylococcus aureus

Staphylococcus epidermidis

Staphylococcus hominis

Staphylococcus haemolyticus

Staphylococcus saprophyticus

Streptococcus species (incl. S. pneumoniae)

Streptococcus pyogenes

Viridans streptococci

Gram-negative aerobes

Acinetobacter species (incl. A. lwoffi)

Aeromonas species (incl. A. hydrophila)

Brucella species

Campylobacter jejuni

Citrobacter species (incl. C. diversus, C. freundii)

Edwardsiella species (incl. E. tarda)

Enterobacter species (incl. E. aerogenes, E. cloacae)

Escherichia coli

Haemophilus influenza

Haemophilus para influenza

Hafnia species

Klebsiella species (incl. K. oxytoca, K. pneumoniae)

Moraxella catarrhalis

Morganella morganii

Neisseria gonorrhea

Pasteurella species (incl. P. multocida)

Proteus mirabilis

Proteus vulgaris

Providencia rettgeri

Providencia stuartii

Pseudomonas aeruginosa

Salmonella species (incl. S. enteritidis, S. typhi)

Serratia marcescens

Shigella species (incl. S. boydii, S. dysenteriae, S. flexneri, S. sonnei)

Vibrio species (incl. V. cholerae, V. parahaemolyticus, V. vulnificus)

Yersinia species (incl. Y. enterocolitica)

Anaerobic microorganisms:

Listeria species

Plesiomonas species

Streptococcus faecalis

The following organisms display varying degrees of in vitro sensitivity to Ciprofloxacin: Alcaligenes, *Enterococcus faecalis*, Flavobacterium, Gardnerella, Legionella, *Mycobacterium fortuitum*, *Mycobacterium tuberculosis*, *Mycoplasma hominis*, *Streptococcus agalactiae,* and Chlamydia.
The following organisms are usually resistant: *Enterococcus faecium, Nocardia asteroides* and *Ureaplasma urealyticum.*

With a few exceptions (see above) anaerobic organisms are moderately sensitive (e.g. Strepto coccus, Peptostreptococcus) to resistant (e.g. Bacteroides, Treponema pallidum).

Pharmacokinetics
Peak plasma concentrations, which are dose-related, are attained 0.5 to 2 hours after oral dosing. Oral bioavailability is approximately 75% with insignificant first pass metabolism. Plasma protein binding is low. Ciprofloxacin is distributed widely throughout the body with extensive tissue penetration, including bone, cartilage, fat, lung, muscle, prostate and skin. It is also present in the aqueous humor of the eye, cerebrospinal fluid, nasal, and bronchial secretions, sputum, saliva, peritoneal fluid, bile secretions, prostatic secretions, and lymph and skin blister fluid. Once steady state has been reached, no accumulation occurs.
Ciprofloxacin is eliminated principally by urinary excretion (mainly during the first 12 hours) and is virtually complete within 24 hours. The rest undergoes biliary excretion and transluminal intestinal secretion.
About 40 to 50% of an oral dose is excreted unchanged in the urine and about 15% as metabolites. The metabolites have antimicrobial activity, but are less active than unchanged Ciprofloxacin. The elimination half-life is 3-5 hours.

Indications

- Urinary tract infections lower respiratory tract infections, gastro-intestinal infections, bone, and joint, skin, and soft tissue infections (caused by Ciprofloxacin sensitive bacteria).
- Gonorrhea (Ciprofloxacin is not effective against Treponema pallidum)
- An aminoglycoside must be administered with Ciprofloxacin in the treatment of infections caused by Pseudomonas aeruginosa.

Contraindications

Safety in pregnancy and lactation has not been established.

- Ciprofloxacin is contra-indicated in children under 18 years and growing adolescents (except where the benefits of treatment outweigh the risks). Experimental studies have shown species variable reversible lesions of the cartilage of weight-bearing joints in immature members of certain animal species.
- Ciprofloxacin is also contra-indicated in patients with hypersensitivity to Ciprofloxacin or any other quinolones.

Warnings

Ciprofloxacin should be used with caution in patients with epilepsy or a history of CNS disorders. Crystalluria has been observed in association with Ciprofloxacin use. Patients on Ciprofloxacin should therefore be well hydrated and must avoid excessive alkalinity of the urine.

Adverse Reactions

The most common adverse events are nausea, diarrhea, vomiting, abdominal pain/discomfort, headache, restlessness, dizziness, and rash. The following additional events have occurred in patients on Ciprofloxacin:

Cardiovascular
Palpitations, tachycardia, syncope, migraine, and vasculitis.

Central Nervous System
Agitation, trembling, tiredness and, infrequently, light headedness, insomnia, hallucinations, delirium, seizures (predominantly in patients who were also receiving theophylline or a non-steroidal anti-inflammatory drug), confusion, dysphasia, myoclonus, nystagmus, toxic psychosis, nightmares, ataxia, lethargy, drowsiness, weakness, malaise, paresthesia, depression, sweating, increase in intracranial pressure, headache, nervousness, peripheral paraplegia, unsteady gait and anxiety states.

Gastro-intestinal
Dyspepsia, flatulence, anorexia, constipation, jaundice, pancreatitis, aphthous ulcers, and dysphagia. Consider pseudomembranous colitis if severe and persistent diarrhoea occurs during or after treatment. In these events Ciprofloxacin must be discontinued and appropriate treatment started immediately.

Hemopoietic
Leucopenia, granulocytopenia, eosinophilia, thrombocytopenia, anaemia and, in very rare cases, agranulocytosis, hemolytic anaemia, methemoglobinemia, prolongation of prothrombin time, leucocytosis and thrombocytosis.

Musculoskeletal
Arthralgia, joint swelling and, in rare cases, myalgia, tendinitis (including achillotendinitis), tendon rupture, exacerbation of gout and general feeling of weakness.

Renal/Urogenital
Vaginitis, vaginal pruritus, candidiasis, and transient renal impairment, including transient renal failure.

Skin/Hypersensitivity reactions
Rashes, including photosensitivity reactions, pruritus, urticaria, flushing and, in less frequent cases, drug fever, petechiae, haemorrhagic bullae, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell syndrome and vasculitis.

Anaphylactic or anaphylactoid reactions, which can present with angioedema, oedema of the face, neck, lips, conjunctivae, larynx or hands, dyspnoea and shock, have been reported rarely. Interstitial nephritis, hepatitis, and hepatic necrosis.

Special senses
Blurred vision, disturbed vision (including colour perception, photophobia, diplopia), tinnitus, hearing loss, impaired or bad taste and anosmia (is a lack of olfaction, or in other words, an inability to perceive smells. It can be either temporary or permanent.).

Laboratory changes
There can be temporary elevations of the following: ALT, AST, alkaline phosphatase, LDH, serum bilirubin, serum creatinine, urea, serum glucose, GGT, serum amylase, uric acid. Crystalluria and

haematuria have been reported.

Precautions

Alkalinity of the urine should be avoided in patients receiving Ciprofloxacin, as this may predispose to crystalluria.
Excessive sunlight should be avoided to avoid the possibility of phototoxicity, manifested as an exaggerated sunburn reaction.

Ciprofloxacin should be used with caution in patients with known or suspected CNS disorders that may predispose to seizures or lower the seizure threshold (e.g. cerebral arteriosclerosis, epilepsy), or in the presence of other risk factors that may predispose to seizures or lower the seizure threshold (e.g. certain drugs, renal impairment).
Long-term or repeated administration of Ciprofloxacin can lead to super infections with resistant bacteria or yeast-like fungi.

Even when the medicine is taken as prescribed; it can affect the speed of reaction to such an extent that the ability to drive and to operate machinery is impaired. Particularly in combination with alcohol.

Drug Interactions

Theophylline
Concomitant administration may lead to an increased risk of theophylline-related adverse reactions (e.g. tachyarrhythmias, cardiac arrest, seizures, and respiratory failure) due to elevated serum concentrations of theophylline and prolongation of its half-life. If this cannot be avoided, serum levels of theophylline should be monitored and the dosage adjusted appropriately.

Non-steroidal anti-inflammatory drugs: There have been reports of potentiation of the CNS stimulant effects and lowering of the seizure threshold when fenbufen was co-administered with quinolones.

Minerals
Concurrent administration with antacids containing magnesium, aluminum, calcium or sucralfate, or divalent or trivalent cations such as iron may substantially interfere with the absorption of Ciprofloxacin. Ciprofloxacin should therefore be administered 1-2 hours before or at least 4 hours after these preparations.

Glibenclamide
The action of this sulfonylurea can be intensified, resulting in hypoglycemia.

Warfarin
The effects of warfarin and its derivatives may be enhanced. When administered concomitantly, coagulation tests should be closely monitored.

Probenecid
Ciprofloxacin serum concentrations will be elevated due to reduced renal secretion.

Cyclosporine
Transient elevations in serum creatinine have been observed in patients on concomitant Ciprofloxacin and cyclosporine.

Metoclopramide
Has been shown to accelerate the absorption of Ciprofloxacin, reducing the time to reach maximum plasma concentrations. No effect was seen on the overall bioavailability of Ciprofloxacin.

Others
Ciprofloxacin has been shown to increase the half-life of caffeine, and to alter serum levels of phenytoin (increase or decrease).

Dosage and Administration

Ceproxx tablets should be swallowed with a full glass (240 ml) of water and may be taken with or without meals.
The usual oral dose is 250 to 750 mg (base) every 12 hours for three to fourteen days. Generally, treatment should be continued for at least 3 days after the signs and symptoms of the infection have disappeared. Severe and/or complicated infections may require prolonged therapy.
A minimum of ten days treatment is recommended for any infections caused by streptococci, due to the risk of late complications.

Adults
Usual adult prescribing limit: Up to 1.5 g (base) daily.

Lower respiratory tract
Mild/moderate - 250-500 mg 12 hourly, 7 to 14 days
Severe/complicated - 750 mg 12 hourly, 7 to 14 days.

Cystic fibrosis
For acute exacerbations of cystic fibrosis, associated with *Pseudomonas aeruginosa* infection, Ciprofloxacin may be given to adolescents and children aged 5 years or more in a dose of 20 mg per kg by mouth daily, up to a maximum of 750 mg twice daily.

Infectious diarrhea
500 mg 12 hourly, 5 to 7 days.

Typhoid fever
500 mg 12 hourly, 10 days.

Intra-abdominal
Complicated - 500 mg 12 hourly, 7 to 14 days (in conjunction with metronidazole).

Urinary tract
Acute uncomplicated cystitis - 250 mg 12 hourly, 3 days.
Mild/moderate - 250 mg 12 hourly, 7 to 14 days.
Severe/complicated - 500 mg 12 hourly, 7 to 14 days.

Chronic bacterial Prostatitis
500 mg 12 hourly, 28 days.

Urethral and endocervical gonorrhea
250 mg as a single dose.

Skin and soft tissue
Mild/moderate - 500 mg 12 hourly, 7 to 14 days.
Severe/complicated - 750 mg 12 hourly, 7 to 14 days.

Bone and joint
Mild/moderate - 500 mg 12 hourly, 4 to 6 weeks or longer.
Severe/complicated - 750 mg 12 hourly, 4 to 6 weeks or longer.

Elderly patients
Should receive a dose as low as possible, depending on the severity of the illness and on the creatinine clearance.

Impaired renal or hepatic function
No dosage adjustment is necessary in patients with hepatic impairment.

The following table provides dosage guidelines for use in patients with renal impairment; however, monitoring of drug serum levels provides the most reliable basis for dosage adjustment:

Creatinine Clearance (ml/min)(ml/sec)	**Dose (base)**
>50/0.83	See Usual adult dose
30-50/0.50-0.83	250-500 mg every 12 hours
5-29/0.08-0.48	250-500 mg every 18 hours
Hemodialysis or Peritoneal dialysis patients	250-500 mg every 24 hours after dialysis

Over Dosage

Reversible renal toxicity has been reported in the case of oral over dosage.
Renal function should be monitored and Mg or Ca containing antacids administered which reduce the absorption of Ciprofloxacin. Treatment should be symptomatic and supportive.

Presentation

Ceproxx 250 mg
Box of 20 tablets

Ceproxx 500 mg
Box of 10 tablets