CIPROXIR®

Ciprofloxacin

Description
Ciproxir® is a broad spectrum antibiotic of fluoroquinolones group.

Clinical pharmacology
The bactericidal action of Ciproxir® results from inhibition of the enzymes topoisomerase II (DNA gyrase) and topoisomerase IV, which are required for bacterial DNA replication, transcription, repair and recombination. The mechanism of action of fluoroquinolones, including Ciproxir®, is different from that of penicillins, cephalosporins, aminoglycosidase, macrolides, and tetracyclines; there fore, microorganisms resistant to these classes of drugs may be susceptible to Ciprofloxacin and other quinolones, there is no known cross –resistance between Ciprofloxacin and other classes of antimicrobials.

Antibacterial activity
Ciproxir® has in vitro activity against a wide range of gram-negative and gram-positive microorganisms.

Aerobic gram –positive microorganisms
Enterococcus faecalis, Staphylococcus aureus , Staphylococcus epidermidis , Staphylococcus saprophyticus , Streptococcus pneumoniae , Streptococcus pyogenes.

Aerobic gram –negative microorganisms
Compylobacter jejuni , Citrobacter diversus , Citrobacter freundi, Enterobacter cloacae , Escherichia coli , Haemophilus influenzae, Haemophilus parainfluenzae , Klebsiella pneumoniae , Moraxella catarrhalis , Morganella morganii, Neisseria gonorrhoese , Proteus vulgaris , Providencia rettgeri , Providencia stuartii , Pseudomonas aeruginosa , Salmonella typhi , Serratia marcescens, Shigella boydii , Shigella dysenteriae, Shigella flexneri, Shigella sonnei.

In invitro:

Aerobic gram-positive microorganisms
Staphylococcus haemolyticus, Staphylococcus hominis, Streptococcus pneumoniae

Aerobic gram-negative microorganisms
Acinetobacter lwoff , Aeromonas hydrophila , Edwardsiella tarda , Enterobacter aerogenes , klebsiella oxytoca , legionella pneumophila , Pasteurella multocido , Salmonella enteritidis , Vibrio cholerae ,Vibrio vulnificus , Yersinia enterocolitica.

Pharmacokinetics

Oral absorption	rapidly (70%)
Presystemic metabolism	----
Plasma half – life	4h
Distribution	widely distributed
Plasma protein binding	20-40%

Indication
1- Urinary tract infection
2- Acute uncomplicated cystitis in females
3- Chronic bacterial prostatitis
4- Lower respiratory tract infections
5- Acute sinusitis
6- Bone and joint infection
7- Complicated intra-abdominal infections
8- Infectious diarrhea
9- Typhoid fever
10- Uncomplicated cervical and urethral gonorrhea
11- Inhalational anthrax

Contraindication
- Ciproxir® is contraindicated in person with a history of hypersensitivity to Ciprofloxacin or any member of the quinolone class of antimicrobial agents.
- Concomitant administration with Tizanidine is contraindicated.

Precaution
- Crystals of Ciproxir® have been observed rarely in the urine of human. Crystalluria related to Ciprofloxacin has been reported only rarely in human urine is usually acidic alkalinity of the urine should be avoided in patients receiving Ciprofloxacin. Patients should be well hydrated to prevent the formation of highly concentrated urine.
- Ciproxir® , may also cause central nervous system (CNS) events , including : nervousness , agitation , insomnia , anxiety nightmares or paranoia.
- Alteration of the dosage regimen is necessary for patient with impairment of renal function.
- Moderate to severe phototoxicity manifested as an exaggerated sunburn reaction has been observed in patients who are exposed to direct sunlight while receiving some members of the quinolone class of drug. Excessive sunlight should be avoided; therapy should be discontinued if phototoxicity occurs.
- As with any potent drug, periodic assessment of organ system functions, including renal, hepatic, and hematopoietic function, is advisable during prolonged therapy.
- Prescribing Ciproxir® tablets in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug- resistant bacteria.

Pregnancy
Pregnancy category C
There are no adequate and well-controlled studies in pregnant women. Use during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Breast feeding
Ciproxir® is excreted in human milk, because of the potential for serious adverse reaction in infants nursing from mothers taking Ciproxir®; 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.

Dosage
Usual adult dose
- **Anthrax, inhalational (treatment):** 500 mg (base) every 12 hours for 60 days.
- **Bone and joint infection:** Mild or moderate- 500 mg (base) every 12 hours for at least four to six weeks.
Sever or complicated- 750 mg (base) every 12 hours for at least four to six weeks.
- **Infectious Diarrhea:** Mild to severe- 500 mg (base) every 12 hours for five to seven days
- **Gonorrhea, endocervical and urethral-** 250 mg (base) as a single dose.
- **Intra abdominal infection-** 500 mg (base) every 12 hours for seven to fourteen days, in combination with oral Metronidazole.
- **Lower respiratory tract infection-**Mild to moderate- 500mg (base) every 12 hours for seven to fourteen days.
Severe or complicated- 750 mg (base) every 12 hours for seven to fourteen days.
- **Meningococcal carriers-** 750 mg (base) as a single dose.
- **Prostatis, chronic-** Mild or moderate: 500 mg (base) every 12 hours for twenty eight days.
- **Sinusitis-** Mild or moderate or typhoid fever- 500 mg (base) every 12 hours for ten days.
- **Skin and soft tissue infections-** Mild or moderate- 500 mg (base) every 12 hours for seven to fourteen days.
Severe or complicated: 750 mg (base) 12 hours for seven to fourteen days.
- **Urinary tract infections-**Acute uncomplicated: 100 mg (base) every 12 hours for three days.
Mild or moderate: 250 mg (base) every 12 hours for seven to fourteen days.
Severe or complicated: 500 mg (base) every 12 hours for seven to fourteen days.

Note: Adults with impaired renal function may require a reduction in dose as follows:

Creatinine clearance (ml/min)/ (ml/sec)	Dose (base)
>50/0.83	See usual adult dose
30-50/0.5-0.83	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

In patients with severe infection and severe renal function impairment, a unit dose of 750 mg may be administered at the intervals noted above; however, these patients should be monitored carefully and serum concentrations of Ciprofloxacin should be measured periodically.

Usual adult prescribing limits
1.5 grams (base) daily

Usual pediatric dose
Children up to 18 years of age - Ciproxir® has been given to pediatric patients, as indicated below, when alternative therapy could not be used. Based on pharmacokinetic studies, dosing for patients with cystic fibrosis should be higher and at more frequent intervals than for patients without cystic fibrosis. Dosing for cystic fibrosis patients also should be decreased as body weight increases.

Anthrax, inhalational (treatment) - 15 mg per kg of body weight per dose (base), not to exceed 500 mg per dose, every 12 hours for 60 days

Cystic fibrosis, pulmonary exacerbations- For children 14 to 28 kg of body weight; 28 to 20 mg (base) per kg of body weight every twelve hours, up to 2 grams per day
For children 28 to 42 kg of body weight : 20 to 15 mg (base) per kg of body weight every twelve hours, up to 2 grams per day

For other infections- 10 to 15 mg (base) per kg of body weight twice a day, up to 1.5 grams per day.

Usual geriatric dose
Dosing is the same as adult dose

Patient consultation
- Ciproxir® should only be used to treat bacterial infections it doesn't treat viral infections (e.g., the common cold). When Ciproxir® is prescribed to treat a bacterial infection; patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping dose or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treated by Ciproxir® or other antibacterial drugs in the future.
- Ciproxir® may be taken with or without meals and to drink fluids liberally. As with other quinolones, concurrent administration of Ciproxir® with magnesium /aluminium antacids , or Sucralfate , Didanosine chewable / buffered tablets or pediatric powder , other highly buffered drugs or with other products containing calcium , Iron or zinc should be avoided. Ciproxir® may be taken two hours before or six hours after taking these products. Ciproxir® should not be taken with dairy products (like milk or yogurt) or calcium fortified juices alone since absorption of Ciproxir® may be significantly reduced; however, Ciproxir® may be taken with a meal that contains these products.
- Ciproxir® may be associated with hypersensitivity reaction, even fallowing a single dose, and to discontinue the drug at the first sign of a skin rash or other allergic reaction.
- To avoid excessive sunlight or artificial ultraviolet light while receiving Ciproxir® and to discontinue therapy if photoxicity occurs.
- Peripheral neuropathies have been associated with Ciproxir® use. If symptoms of peripheral neuropathy including pain, burning, tingling, numbness and / or weakness develop, they should discontinue treatment and contact their physicians.
- To discontinue treatment, rest and refrain from exercise and inform their physician if they experience pain, inflammatiom, or rupture of a tendon.
- Ciproxir® may cause dizziness and lightheadedness, therefore, patients should know how they react to this drug before they operate an automobile or machinery or engage in activities requiring mental alertness or coordination.
- Ciproxir® may increase the effects of Thephylline and Caffeine. There is a possibility of Caffeine accumulation when products containing Caffeine are consumed while taking quinolones.
- Convulsions have been reported in patients receiving quinolones , including Ciproxir® , and to notify their physician before taking this drug if there is a history of this condition.
- Ciproxir® has been associated with an increased rate of adverse events involving joints and surrounding tissue structures (like tendous) in pediatric patients (less than 18 years of age). Parents should inform their child's physician if the child has a history of joint –related problems before taking this drug. Parents of pediatric patients should also notify their child's physician of any joint related problems that occur during or following Ciproxir® therapy.

Warning
- The safety and effectiveness of Ciproxir® in pregnant and lactating woman have not been established.
- Safety and effectiveness in pediatric patients and adolescents less than 18 years of age have not been established. Except for use inhalational anthrax (post – exposure)

Interaction
- Concurrent administration of antacids containing Magnesium hydroxide or Aluminum hydroxide may reduce the bioavailability of Ciproxir® by as much as 90%
- The serum concentration of Ciproxir® and Metronidazole were not altered when these two drugs were given concomitantly.
- Concomitant administration of Ciproxir® with Theophylline decreases the clearance of Theophylline resulting in elevated serum Theophylline levels and increased risk of a patient developing CNS or other adverse reactions.
- Ciproxir® decreases Caffeine clearance and inhibits the formation of paraxanthine after Caffeine administration
- Altered serum levels of Phenytoin have been reported in patients receiving concomitant Ciproxir®
- The concomitant administration of Ciproxir® with the sulfonylurea glyburide has, on rare occasions, resulted in severe hypoglycemia.
- Ciproxir® has been reported to enhance the effects of the oral anticoagulant Warfarin or its derivatives.

Laboratory value alteration
Administration of Ciproxir® may change the following physiology /laboratory test values : Elevated white blood cells (10.1%) , increased/decreased white blood cells , increased a PTT , blood urea nitrogen , increased calcium , creatinine , eosinophils , serum lipase , neutrophils , urine glucose , urine protein , urine red blood cells , urine white blood cells , decreased albumin , creatinine clearance , hematocrit , hemoglobin ,lymphocytes , phosphorus , red blood cells , sodium (<1%)

Adverse reactions
Incidence more frequent
Nausea, diarrhea, vomiting, abdominal pain/discomfort, headache, restlessness, rash

Incidence less frequent (< 1%)
Foot pain, palpitation, atrialmflutter, syncope, hypertension , cerebral, dizziness, insomnia, nightmares, halucinations, manic reaction, tremor, anorexia, paresthesia, depression, dysphagia, gastrointestinal bleeding, polyuria, urinary retention, vaginities, acidosis, pruritus, urticaria, photosensitivity, flushing, fever, chills, hyperpigmentation, blurred vision, eye pain, diplopia, tinnitus

Overdose
The stomach should be emptied by inducing vomiting or by gastric lavage. The patient should be carefully observed and given supportive treatment, including monitoring of renal function and administration of magnesium, aluminum, or calcium containing antacids which can reduce the absorption of Ciproxir®. Adequate hydration must be maintained.

Storage and stability condition
- Store below 30°C.
- Protect from light and moisture.
- Keep out of the reach of children.

Packaging
Film coated tablets containing 250 or 500 mg of Ciprofloxacin hydrochloride.

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