Kinoxin® Tablets
Ciprofloxacin hydrochloride

DESCRIPTION
Kinoxin® (ciprofloxacin hydrochloride) Tablets are synthetic broad spectrum antimicrobial agents, belonging to the quinolone group, for oral administration.
Kinoxin® film-coated tablets are available in 250 mg and 500 mg (ciprofloxacin equivalent) strengths. The inactive ingredients are starch, microcrystalline cellulose, silicone dioxide, crospovidone, magnesium stearate, croscarmellose sodium, hydroxypropyl methylcellulose, titanium dioxide, polyethylene glycol and water.

INDICATIONS AND USAGE
Kinoxin® is indicated for the treatment of infections caused by susceptible strains of the designated microorganisms in the conditions listed below. Please see **DOSAGE AND ADMINISTRATION** for specific recommendations.
Acute Sinusitis caused by *Haemophilus influenzae, Streptococcus pneumoniae,* or *Moraxella catarrhalis*.
Lower Respiratory Tract Infections caused by *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Proteus mirabilis, Pseudomonas aeruginosa, Haemophilus influenzae, Haemophilus parainfluenzae,* or *Streptococcus pneumoniae.* Also *Moraxella catarrhalis* for the treatment of acute exacerbations of chronic bronchitis.
Note: Although effective in clinical trials, ciprofloxacin is not a drug of first choice in the treatment of presumed or confirmed pneumonia secondary to *Streptococcus pneumoniae.*
Urinary Tract Infections caused by *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Serratia marcescens, Proteus mirabilis, Providencia rettgeri, Morganella morganii, Citrobacter freundii, Pseudomonas aeruginosa, Staphylococcus epidermidis, Staphylococcus saprophyticus,* or *Enterococcus faecalis.*
Acute Uncomplicated Cystitis in females *caused by Escherichia coli or Staphylococcus saprophyticus.* (See **DOSAGE AND ADMINISTRATION**.)
Chronic Bacterial Prostatitis caused by *Escherichia coli* or *Proteus mirabilis.*
Complicated Intra-Abdominal Infections (used in combination with metronidazole) caused by *Escherichia coli, Pseudomonas aeruginosa, Proteus mirabilis, Klebsiella pneumoniae,* or *Bacteroides fragilis.* (See **DOSAGE AND ADMINISTRATION**.)
Skin and Skin Structure Infections caused by *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Proteus mirabilis, Proteus vulgaris, Providencia stuartii, Morganella morganii, Citrobacter freundii, Pseudomonas aeruginosa, Staphylococcus aureus* (methicillin susceptible), *Staphylococcus epidermidis,* or *Streptococcus pyogenes.*
Bone and Joint Infections caused by *Enterobacter cloacae, Serratia marcescens,* or *Pseudomonas aeruginosa.*
Infectious Diarrhea caused by *Escherichia coli* (enterotoxigenic strains), *Campylobacter jejuni, Shigella boydii*, Shigella dysenteriae, Shigella flexneri* or *Shigella sonnei** when antibacterial therapy is indicated.
Typhoid Fever (Enteric Fever) caused by *Salmonella typhi.*
NOTE: The efficacy of ciprofloxacin in the eradication of the chronic typhoid carrier state has not been demonstrated.
Uncomplicated cervical and urethral gonorrhea due to *Neisseria gonorrhoeae.*
Inhalational anthrax (post-exposure): To reduce the incidence or progression of disease following exposure to aerosolized *Bacillus anthracis.*
Ciprofloxacin serum concentrations achieved in humans serve as a surrogate endpoint reasonably likely to predict clinical benefit and provide the basis for this indication. (See also, **INHALATION ANTHRAX - ADDITIONAL INFORMATION**).
- Although treatment of infections due to this organism in this organ system demonstrated a clinically significant outcome, efficacy was studied in fewer than 10 patients.
If anaerobic organisms are suspected of contributing to the infection, appropriate therapy should be administered.
Appropriate culture and susceptibility tests should be performed before treatment in order to isolate and identify organisms causing infection and to determine their susceptibility to ciprofloxacin. Therapy with Kinoxin® may be initiated before results of these tests are known; once results become available, appropriate therapy should be continued. As with other drugs, some strains of *Pseudomonas aeruginosa* may develop resistance fairly rapidly during treatment with ciprofloxacin. Culture and susceptibility testing performed periodically during therapy will provide information not only on the therapeutic effect of the antimicrobial agent but also on the possible emergence of bacterial resistance.
Kinoxin® (ciprofloxacin hydrochloride) is contraindicated in persons with a history of hypersensitivity to ciprofloxacin or any member of the quinolone class of antimicrobial agents.

WARNINGS
THE SAFETY AND EFFECTIVENESS OF CIPROFLOXACIN IN PEDIATRIC PATIENTS AND ADOLESCENTS (LESS THAN 18 YEARS OF AGE), - EXCEPT FOR USE IN INHALATIONAL ANTHRAX (POST- EXPOSURE), AND LACTATING WOMEN HAVE NOT BEEN ESTABLISHED. (See **PRECAUTIONS: Pediatric Use, Pregnancy,** and **Nursing Mothers** subsections.) Convulsions, increased intracranial pressure, and toxic psychosis have been reported in patients receiving quinolones, including ciprofloxacin. Ciprofloxacin may also cause central nervous system (CNS) events including: dizziness, confusion, tremors, hallucinations, depression, and, rarely, suicidal thoughts or acts. These reactions may occur following the first dose. If these reactions occur in patients receiving ciprofloxacin, the drug should be discontinued and appropriate measures instituted. As with all quinolones, 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. severe cerebral arteriosclerosis, epilepsy), or in the presence of other risk factors that may predispose to seizures or lower the seizure threshold (e.g. certain drug therapy, renal dysfunction). (See **PRECAUTIONS: General, Information for Patients, Drug Interactions** and **ADVERSE REACTIONS**.)
SERIOUS AND FATAL REACTIONS HAVE BEEN REPORTED IN PATIENTS RECEIVING CONCURRENT ADMINISTRATION OF CIPROFLOXACIN AND THEOPHYLLINE. These reactions have included cardiac arrest, seizure, status epilepticus, and respiratory failure. Although similar serious adverse effects have been reported in patients receiving theophylline alone, the possibility that these reactions may be potentiated by ciprofloxacin cannot be eliminated. If concomitant use cannot be avoided, serum levels of theophylline should be monitored and dosage adjustments made as appropriate.
Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving quinolone therapy. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, tingling, pharyngeal or facial edema, dyspnea, urticaria, and itching. Only a few patients had a history of hypersensitivity reactions. Serious anaphylactic reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway management, including intubation, should be administered as indicated.
Severe hypersensitivity reactions characterized by rash, fever, eosinophilia, jaundice, and hepatic necrosis with fatal outcome have also been rarely reported in patients receiving ciprofloxacin along with other drugs. The possibility that these reactions were related to ciprofloxacin cannot be excluded. Ciprofloxacin should be discontinued at the first appearance of a skin rash or any other sign of hypersensitivity.
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including ciprofloxacin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.
Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of "antibiotic-associated colitis."
After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *C. difficile* colitis.
Achilles and other tendon ruptures that required surgical repair or resulted in prolonged disability have been reported with ciprofloxacin and other quinolones. Ciprofloxacin should be discontinued if the patient experiences pain, inflammation, or rupture of a tendon.
Ciprofloxacin has not been shown to be effective in the treatment of syphilis. Antimicrobial agents used in high dose for short periods of time to treat gonorrhea may mask or delay the symptoms of incubating syphilis. All patients with gonorrhea should have a serologic test for syphilis after three months.

PRECAUTIONS
General: Crystals of ciprofloxacin have been observed rarely in the urine of human subjects. Alkalinity of the urine should be avoided in patients receiving ciprofloxacin. Patients should be well hydrated to prevent the formation of highly concentrated urine.
Quinolones, including ciprofloxacin, may also cause central nervous system (CNS) events, including: nervousness, agitation, insomnia, anxiety, nightmares or paranoia. (See **WARNINGS**, **Information for Patients,** and **Drug Interactions.)** Alteration of the dosage regimen is necessary for patients with impairment of renal function. (See **DOSAGE AND ADMINISTRATION.**)
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 drugs. 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, is advisable during prolonged therapy.
Information for Patients: Patients should be advised:
- that ciprofloxacin may be taken with or without meals and to drink fluids liberally. As with other quinolones, concurrent administration of ciprofloxacin with magnesium/aluminium antacids, or sucralfate, (didanosine) chewable/buffered tablets or pediatric powder, or with other products containing calcium, iron or zinc should be avoided. These products may be taken two hours after or six hours before ciprofloxacin. Ciprofloxacin should not be taken concurrently with milk or yogurt alone, since absorption of ciprofloxacin may be significantly reduced. Dietary calcium as a part of a meal, however, does not significantly affect ciprofloxacin absorption.
- that ciprofloxacin may be associated with hypersensitivity reactions, even following 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 ciprofloxacin and to discontinue therapy if phototoxicity occurs.
- to discontinue treatment; rest and refrain from exercise; and inform their physician if they experience pain, inflammation, or rupture of a tendon.
- that ciprofloxacin 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.
- that ciprofloxacin may increase the effects of theophylline and caffeine. There is a possibility of caffeine accumulation when products containing caffeine are consumed while taking quinolones.
- that convulsions have been reported in patients taking quinolones, including ciprofloxacin, and to notify their physician before taking the drug if there is a history of this condition.
Drug Interactions: As with some other quinolones, concurrent administration of ciprofloxacin with theophylline may lead to elevated serum concentrations of theophylline and prolongation of its elimination half-life. This may result in increased risk of theophylline-related adverse reactions. (See **WARNINGS**.) If concomitant use cannot be avoided, serum levels of theophylline should be monitored and dosage adjustments made as appropriate.
Histamine H_2-receptor antagonists appear to have no significant effect on the bioavailability of ciprofloxacin.

Altered serum levels of phenytoin (increased and decreased) have been reported in patients receiving concomitant ciprofloxacin.
The concomitant administration of ciprofloxacin with the sulfonylurea glyburide has, on rare occasions, resulted in severe hypoglycemia.
Some quinolones, including ciprofloxacin, have been associated with transient elevations in serum creatinine in patients receiving cyclosporine concomitantly.
Quinolones have been reported to enhance the effects of the oral anticoagulant warfarin or its derivatives. When these products are administered concomitantly, prothrombin time or other suitable coagulation tests should be closely monitored.
Probenecid interferes with renal tubular secretion of ciprofloxacin and produces an increase in the level of ciprofloxacin in the serum. This should be considered if patients are receiving both drugs concomitantly.
As with other broad spectrum antimicrobial agents, prolonged use of ciprofloxacin may result in overgrowth of nonsusceptible organisms.
Repeated evaluation of the patient's condition and microbial susceptibility testing is essential. If superinfection occurs during therapy, appropriate measures should be taken.
Pregnancy: There are no adequate and well-controlled studies in pregnant women. Ciprofloxacin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Nursing Mothers: Ciprofloxacin is excreted in human milk. Because of the potential for serious adverse reactions in infants nursing from mothers taking ciprofloxacin, 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.
Pediatric Use: Safety and effectiveness in pediatric patients and adolescents less than 18 years of age have not been established, except for use in inhalational anthrax (post-exposure).
For the indication of inhalational anthrax (post-exposure), the risk-benefit assessment indicates that administration of ciprofloxacin to pediatric patient is appropriate. For information regarding pediatric dosing in inhalational anthrax (post-exposure), see **DOSAGE AND ADMINISTRATION** and **INHALATIONAL ANTHRAX - ADDITIONAL INFORMATION.**
Geriatric Use: Ciprofloxacin is known to be substantially excreted by the kidney, and the risk of adverse reactions may be geater in patients with impaired renal function. No alteration of dosage is necessary for patients greater than 65 years of age with normal renal function.
However, since some older individuals experience reduced renal function by virtue of their advanced age, care should be taken in dose selection for elderly patients, and renal function monitoring may be useful in these patients.

ADVERSE REACTIONS

The most frequent adverse events reported in the clinical trials were nausea (5.2%), diarrhea (2.3%), vomiting (2%), abdominal pain/discomfort (1.7%), headache (1.2%), restlessness (1.1%), and rash (1.1%).
Other less frequent adverse events observed in the clinical trials and post marketing are listed below:
CARDIOVASCULAR: Palpitation, atrial flutter, ventricular ectopy, syncope, hypertension, angina pectoris, myocardial infarction, cardiopulmonary arrest, cerebral thrombosis, postural hypotension, vasculitis.
CENTRAL NERVOUS SYSTEM: Dizzines, lightheadedness, insomnia, nightmares, hallucinations, manic reaction, irritability, tremor, ataxia, convulsive seizures, lethargy, drowsiness, weakness, malaise, anorexia, phobia, depersonalization, depression, parasthesis, agitation, confusion, delirium, dysphasia, myoclonus, nystagmus, toxic psychosis.
GASTROINTESTINAL: Painful oral mucosa, oral candidiasis, dysphagia, intestinal perforation, gastrointestinal bleeding, cholestatic jaundice, constipation, dyspepsia, flatulence, hepatic necrosis, jaundice, pancreatitis, pseudomembraneous colitis.
MUSCULOSKELETAL: Arthralgia or back pain, joint stiffness, achiness, neck or chest pain, flare up of gout, myalgia, tendinitis/tendon rupture, possible aggravation of myasthenia gravis.
RENAL/UROGENITAL: Interstitial nephritis, nephritis, renal failure, polyuria, urinary retention, urethral bleeding, vaginitis, acidosis, albuminuria, candiduria, renal calculi, vaginal candidiasis.
RESPIRATORY: Dyspnea, epistaxis, laryngeal or pulmonary edema, hiccough, hemoptysis, bronchospasm, pulmonary embolism.
SKIN/HYPERSENSITIVITY: Pruritus, urticaria, photosensitivity, flushing, fever, chills, angioedema, edema of the face, neck, lips, conjunctivae or hands, cutaneous candidiasis, hyperpigmentation, erythema nodosum, anaphylactic reactions, erythema multiforme/Stevens-Johnson syndrome, exfoliative dermatitis, toxic epidermal necrolysis.
SPECIAL SENSES: Blurred vision, disturbed vision (change in color perception, overbrightness of lights), decreased visual acuity, diplopia, eye pain, tinnitus, hearing loss, bad taste, aosmia, taste loss.
Adverse Laboratory Changes: Changes in laboratory parameters listed as adverse events without regard to drug relationship are listed below:
Hepatic: Elevations of ALT (SGPT) (1.9%), AST (SGOT) (1.7%), alkaline phosphatase (0.8%), LDH (0.4%), serum bilirubin (0.3%).
Hematologic: Eosinophilia (0.6%), leukopenia (0.4%), decreased platelets (0.1%), elevated blood platelets (0.1%), pancytopenia (0.1%)
Renal: Elevations of serum creatinine (1.1%), BUN (0.9%), crystalluria, cylindruria and hematuria.

OVERDOSAGE

In the event of acute overdosage, the stomach should be emptied by inducing vomiting or by gastric lavage. The patient should be carefully observed and given supportive treatment. Adequate hydration must be maintained. Only a small amount of ciprofloxacin (<10%) is removed from the body after hemodialysis or peritoneal dialysis.

DOSAGE AND ADMINISTRATION

The recommended adult dosage for acute sinusitis is 500 mg every 12 hours.
Lower respiratory tract infections may be treated with 500 mg every 12 hours. For more severe or complicated infections, a dosage of 750 mg may be given every 12 hours.
Severe/complicated urinary tract infections or urinary tract infections caused by organisms not highly susceptible to ciprofloxacin may be treated with 500 mg every 12 hours. For other mild/moderate urinary infections, the usual adult dosage is 250 mg every 12 hours.
In acute uncomplicated cystitis in females, the usual dosage is 100 mg or 250 mg every 12 hours. For acute uncomplicated cystitis in females, 3 days of treatment is recommended while 7 to 14 days is suggested for other mild/moderate, severe or complicated urinary tract infections.
The recommended adult dosage for chronic bacterial prostatitis is 500 mg every 12 hours.
The recommended adult dosage for oral sequential therapy of complicated intra-abdominal infections is 500 mg every 12 hours. (To provide appropriate anaerobic activity, metronidazole should be given according to product labeling.)
Skin and skin structure infections and bone and joint infections may be treated with 500 mg every 12 hours. For more severe or complicated infections, a dosage of 750 mg may be given every 12 hours.
The recommended adult dosage for infectious diarrhea or typhoid fever is 500 mg every 12 hours. For the treatment of uncomplicated urethral and cervical gonococcal infections, a single 250 mg dose is recommended.

DOSAGE GUIDELINE

Infection	Type or Severity	Unit Dose	Frequency	Usual durations*
Acute sinusitis	Mild/Moderate	500 mg	q 12 h	10 Days
Lower	Mild/Moderate	500 mg	q 12 h	7 to 14 Days
Respiratory Tract	Severe/Complicated	750 mg	q 12 h	7 to 14 Days
Urinary Tract	Acute Uncomplicated	100 mg or 250 mg	q 12 h	3 Days
	Mild/Moderate	250 mg	q 12 h	7 to 14 Days
	Severe/Complicated	500 mg	q 12 h	7 to 14 Days
Chronic Bacterial Prostatitis	Mild/Moderate	500 mg	q 12 h	28 Days
Intra-Abdominal**	Complicated	500 mg	q 12 h	7 to 14 Days
Skin and Skin	Mild/Moderate	500 mg	q 12 h	7 to 14 Days
Structure	Severe/Complicated	750 mg	q 12 h	7 to 14 Days
Bone and Joint	Mild/Moderate	500 mg	q 12 h	>4 to 6 weeks
	Severe/Complicated	750 mg	q 12 h	>4 to 6 weeks
Infectious Diarrhea	Mild/Moderate/Severe	500 mg	q 12 h	5 to 7 Days
Typhoid Fever	Mild/Moderate	500 mg	q 12 h	10 Days
Urethral and Cervical Gonococcal Infections	Uncomplicated	250 mg	single dose	single dose
Inhalational anthrax (post-exposure)***	Adult	500 mg	q 12 h	60 Days
	Pediatric	15mg/Kg per dose, not to exceed 500 mg per dose	q 12 h	60 Days

*Generally ciprofloxacin should be continued for at least 2 days after the signs and symptoms of infection have disappeared, except for inhalation anthrax (post-exposure).
** used in conjuction with metronidazole
*** Drug administration should begin as soon as possible after suspected or confirmed exposure. This indication is based on a surrogate endpoint, ciprofloxacin serum concentrations achieved in humans, reasonably likely to predict clinical benefit. For a discussion of ciprofloxacin serum concentrations in various human populations, see **INHALATIONAL ANTHRAX - ADDITIONAL INFORMATION.**
Complicated Intra-Abdominal Infections: Sequential therapy [parenteral to oral - 400 mg Ciprofloxacin I.V. q 12 h (plus I.V. metronidazole) --> 500 mg Kinoxin® Tablets q 12 h (plus oral metronidazole)] can be instituted at the discretion of the physician. 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 duration of treatment depends upon the severity of infection. Generally ciprofloxacin should be continued for at least 2 days after the signs and symptoms of infection have disappeared.The usual duration is 7 to 14 days; however, for severe and complicated infections more prolonged therapy may be required. Bone and joint infections may require treatment for 4 to 6 weeks or longer. Chronic Bacterial Prostatitis should be treated for 28 days. Infectious diarrhea may be treated for 5-7 days. Typhoid fever should be treated for 10 days.
Impaired Renal Function: Ciprofloxacin is eliminated primarily by renal excretion; however, the drug is also metabolized and partially cleared through the biliary system of the liver and through the intestine. These alternate pathways of drug elimination appear to compensate for the reduced renal excretion in patients with renal impairment. Nonetheless, some modification of dosage is recommended, particularly for patients with severe renal dysfunction. The following table provides dosage guidelines for use in patients with renal impairment; however, monitoring of serum drug levels provides the most reliable basis for dosage adjustment:

RECOMMENDED STARTING AND MAINTENANCE DOSES FOR PATIENTS WITH IMPAIRED RENAL FUNCTION

Creatinine Clearance (mL/min)	Dose
>50	See Usual Dosage.
30-50	250-500 mg q 12 h
5-29	250-500 mg q 18 h
Patients on hemodialysis or Peritoneal dialysis	250-500 mg q 24 h (after dialysis)

In patients with severe infections and severe renal impairment, a dose of 750-mg may be administered at the intervals noted above; however, patients should be carefully monitored and the serum ciprofloxacin concentration should be measured periodically. Peak concentrations (1-2 hours after dosing) should generally range from 2 to 4 µg/mL.
For patients with changing renal function or for patients with renal impairment and hepatic insufficiency, measurement of serum concentrations of ciprofloxacin will provide additional guidance for adjustment dosage.

STORAGE CONDITIONS

Store in a dry place below 25°C, protected from light. Do not refrigerate.

PRESENTATION

Tablets 250 mg and 500 mg in blister pack of 14 's.

Do not use after expiry date.

This is a medicament

-A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
-Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
-The doctor and the pharmacist are experts in medicine, its benefits and risks.
-Do not by yourself interrupt the period of treatment prescribed.
-Do not repeat the same prescription without consulting your doctor.

Keep medicament out of children's reach.

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