

Post marketing reports of adverse drug reactions:

System Organ Class	Adverse Reactions
Body as a Whole	Headache Abdominal Pain/Discomfort Pain
Cardiovascular	QT prolongation Torsade de Pointes Vasculitis and ventricular arrhythmia
Central Nervous System	Hypertonia Myasthenia Exacerbation of myasthenia gravis Peripheral neuropathy Polyneuropathy Twitching
Eye Disorders	Nystagmus
Gastrointestinal	Pseudomembranous colitis
Hemic/Lymphatic	Pancytopenia (life threatening or fatal outcome)
Hepatobiliary	Hepatic failure (including fatal cases)
Infections and Infestations	Candidiasis (oral, gastrointestinal, vaginal)
Investigations	Prothrombin time prolongation or decrease Cholesterol elevation (serum) Potassium elevation (serum)
Musculoskeletal	Myalgia Myoclonus Tendinitis Tendon rupture
Psychiatric Disorders	Agitation Confusion Delirium
Skin/Hypersensitivity	Acute generalize exanthematous pustulosis (AGEP) Fixed eruption Serum sickness-like reaction
Special Senses	Anosmia Hyperesthesia Hypesthesia Taste loss

Laboratory Changes:
Changes in laboratory parameters while on Ciprofloxacin are listed below: Hepatic—Elevations of ALT (SGPT), AST (SGOT), alkaline phosphatase, LDH, serum bilirubin. Hematologic— Eosinophilia, leukopenia, decreased blood platelets, elevated blood platelets, pancytopenia. Renal—Elevations of serum creatinine, BUN, crystalluria, cylindruria, and hematuria have been reported. Other changes occurring were: elevation of serum gammaglutamyl transferase, elevation of serum amylase, reduction in blood glucose, elevated uric acid, decrease in hemoglobin, anemia, bleeding diathesis, increase in blood monocytes, and leukocytosis.

DRUG INTERACTIONS:
Ciprofloxacin is an inhibitor of human cytochrome P450 1A2 (CYP1A2) mediated metabolism. Co- administration of CIPRO with other drugs primarily metabolized by CYP1A2 results in increased plasma concentrations of these drugs and could lead to clinically significant adverse events of the co- administered drug.

Drugs	Recommendation	Comments
Oral antidiabetic drugs	Use with caution Glucose-lowering effect potentiated	Hypoglycemia sometimes severe has been reported when Ciprofloxacin and oral antidiabetic agents, mainly sulfonylureas (for example, glyburide, glimepiride), were co-administered, presumably by intensifying the action of the oral antidiabetic agent. Fatalities have been reported. Monitor blood glucose when Ciprofloxacin is co-administered with oral antidiabetic drugs.
Phenytoin	Use with caution Altered serum levels of phenytoin (increased and decreased)	To avoid the loss of seizure control associated with decreased phenytoin levels and to prevent phenytoin overdose-related adverse reactions upon Ciprofloxacin discontinuation in patients receiving both agents, monitor phenytoin therapy, including phenytoin serum concentration during and shortly after co-administration of Ciprofloxacin with phenytoin.
Cyclosporine	Use with caution (transient elevations in serum creatinine)	Monitor renal function (in particular serum creatinine) when Ciprofloxacin is co-administered with cyclosporine.
Anti-coagulant drugs	Use with caution (Increase in anticoagulant effect)	The risk may vary with the underlying infection, age and general status of the patient so that the contribution of Ciprofloxacin to the increase in INR (international normalized ratio) is difficult to assess. Monitor prothrombin time and INR frequently during and shortly after co-administration of Ciprofloxacin with an oral anti-coagulant (for example, warfarin).
Methotrexate	Use with caution Inhibition of methotrexate renal tubular transport potentially leading to increased methotrexate plasma levels	Potential increase in the risk of methotrexate associated toxic reactions. Therefore, carefully monitor patients under methotrexate therapy when concomitant Ciprofloxacin therapy is indicated.
Ropinirole	Use with caution	Monitoring for ropinirole-related adverse reactions and appropriate dose adjustment of ropinirole is recommended during and shortly after co-administration with Ciprofloxacin.
Clozapine	Use with caution	Careful monitoring of clozapine associated adverse reactions and appropriate adjustment of clozapine dosage during and shortly after co-administration with Ciprofloxacin are advised.
NSAIDs	Use with caution	Non-steroidal anti-inflammatory drugs (but not acetyl salicylic acid) in combination of very high doses of quinolones have been shown to provoke convulsions in pre-clinical studies and in postmarketing.
Sildenafil	Use with caution Two-fold increase in exposure	Monitor for sildenafil toxicity.
Duloxetine	Avoid Use Five-fold increase in duloxetine exposure	If unavoidable, monitor for duloxetine toxicity
Caffeine/Xanthine Derivatives	Use with caution Reduced clearance resulting in elevated levels and prolongation of serum half-life	Ciprofloxacin inhibits the formation of paraxanthine after caffeine administration (or pentoxifylline containing products). Monitor for xanthine toxicity and adjust dose as necessary.

Drug(s) Affecting Pharmacokinetics of Ciprofloxacin		
Antacids, Sucralfate, Multivitamins and Other Products Containing Multivalent Cations (magnesium/aluminum antacids; polymeric phosphate binders (for example, sevelamer, lanthanum carbonate); sucralfate; didanosine) chewable/buffered tablets or pediatric powder; other highly buffered drugs; or products containing calcium, iron, or zinc and dairy products)	Ciprofloxacin should be taken at least two hours before or six hours after Multivalent cation-containing products administration.	Ciprofloxacin inhibits the formation of paraxanthine after caffeine administration (or pentoxifylline containing products). Monitor for xanthine toxicity and adjust dose as necessary.
Probenecid	Use with caution (interferes with renal tubular secretion of Ciprofloxacin and increases Ciprofloxacin serum levels)	Potential of Ciprofloxacin toxicity may occur.

Drugs that are affected by and affecting ciprofloxacin:

Drugs That are Affected by Ciprofloxacin		
Drugs	Recommendation	Comments
Tizanidine	Contraindicated	Concomitant administration of tizanidine and Ciprofloxacin is contraindicated due to the potentiation of hypotensive and sedative effects of tizanidine.
Theophylline	Avoid Use (Plasma Exposure Likely to be Increased and Prolonged)	Concurrent administration of Ciprofloxacin with theophylline may result in increased risk of a patient developing central nervous system (CNS) or other adverse reactions. If concomitant use cannot be avoided, monitor serum levels of theophylline and adjust dosage as appropriate.
Drugs Known to Prolong QT Interval	Avoid Use	Ciprofloxacin may further prolong the QT interval in patients receiving drugs known to prolong the QT interval (for example, class IA or III antiarrhythmics, tricyclic antidepressants, macrolides, antipsychotics) and Use in

CONTRAINDICATIONS:
Hypersensitivity:
Ciprofloxacin is contraindicated in persons with a history of hypersensitivity to ciprofloxacin, any member of the quinolone class of antibacterials, or any of the product components. **Tizanidine** Concomitant administration with tizanidine is contraindicated.

WARNINGS AND PRECAUTIONS:
Disabling and potentially irreversible serious adverse reactions including tendinitis and tendon rupture, peripheral neuropathy, and central nervous system effects:
Fluoroquinolones, including Ciprofloxacin, have been associated with disabling and potentially irreversible serious adverse reactions that include tendinitis, tendon rupture, arthralgia, myalgia, peripheral neuropathy, and central nervous system effects (hallucinations, anxiety, depression, insomnia, severe headaches, and confusion). These reactions can occur within hours to weeks after starting Ciprofloxacin. Discontinue Ciprofloxacin immediately at the first signs or symptoms of any serious adverse reaction.

Tendinitis and tendon rupture:
Fluoroquinolones, including Ciprofloxacin, have been associated with an increased risk of tendinitis and tendon rupture, most frequently involves the Achilles tendon, and has also been reported with the rotator cuff (the shoulder), the hand, the biceps, the thumb, and other tendons. Tendinitis or tendon rupture can occur, within hours or days of starting Ciprofloxacin, or as long as several months after completion of fluoroquinolone therapy. The risk of developing fluoroquinolone-associated tendinitis and tendon rupture is increased in patients over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants.

Peripheral neuropathy:
Fluoroquinolones, including Ciprofloxacin, have been associated with an increased risk of peripheral neuropathy. Cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesias, hypoesthesias, dysesthesias and weakness have been reported in patients receiving fluoroquinolones.

Central nervous system effects:
Fluoroquinolones have been associated with an increased risk of central nervous system (CNS) effects, including.Convulsions, increased intracranial pressure (including pseudotumor cerebri), and toxic psychosis. Ciprofloxacin may also cause central nervous system (CNS) events including: nervousness, agitation,insomnia, anxiety,nightmares, paranoia, dizziness, confusion,tremors,hallucinations,depression, and psychotic reactions have progressed to suicidal ideations/thoughts and self-injurious behavior such as attempted or completed suicide. Use with caution in epileptic patients and patients with known or suspected CNS disorders that may predispose to seizures or lower the seizure threshold. Use Ciprofloxacin when the benefits of treatment exceed the risks, since these patients are endangered because of possible undesirable CNS side effects.

Exacerbation of myasthenia gravis:
Fluoroquinolones have neuromuscular blocking activity and may exacerbate muscle weakness in patients with myasthenia gravis. Postmarketing serious adverse reactions, including deaths and requirement for ventilatory support, have been associated with fluoroquinolone use in patients with myasthenia gravis. Avoid ciprofloxacin in patients with known history of myasthenia gravis.

Other serious and sometimes fatal adverse reactions:
Other serious and sometimes fatal adverse reactions, some due to hypersensitivity, and some due to uncertain etiology, have been reported in patients receiving therapy with quinolones.

Clinical manifestations may include one or more of the following:

- Fever, rash, or severe dermatologic reactions (for example, toxic epidermal necrolysis, Stevens- Johnson syndrome);
- Vasculitis; arthralgia; myalgia; serum sickness;
- Allergic pneumonitis;
- Interstitial nephritis; acute renal insufficiency or failure;
- Hepatitis; jaundice; acute hepatic necrosis or failure; Anemia, including hemolytic and aplastic; thrombocytopenia, including thrombotic thrombocytopenic purpura; leukopenia; agranulocytosis; pancytopenia; and/or other hematologic abnormalities. Discontinue ciprofloxacin immediately at the first appearance of a skin rash, jaundice, or any other sign of hypersensitivity and supportive measures instituted.

Hypersensitivity reactions: Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving fluoroquinolone therapy. Serious anaphylactic reactions require immediate emergency treatment with epinephrine and other resuscitation measures, including oxygen, intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines, and airway management, including intubation, as indicated.

Hepatotoxicity: Cases of severe hepatotoxicity, including hepatic necrosis, life-threatening hepatic failure, and fatal events. Acute liver injury is rapid in onset (range 1–39 days), and is often associated with hypersensitivity. The pattern of injury can be hepatocellular, cholestatic, or mixed. Most patients with fatal outcomes were older than 55 years old. In the event of any signs and symptoms of hepatitis (such as

anorexia, jaundice, dark urine, pruritus, or tender abdomen), discontinue treatment immediately. There can be a temporary increase in transaminases, alkaline phosphatase, or cholestatic jaundice, especially in patients with previous liver damage, who are treated with ciprofloxacin.

Serious adverse reactions with concomitant theophylline: 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. Instances of nausea, vomiting, tremor, irritability, or palpitation have also occurred.

Clostridium difficile-associated diarrhea: Clostridium difficile®, difficile)-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Ciprofloxacin, and may range in severity from mild diarrhea to fatal colitis.

Prolongation of the qt interval: Some fluoroquinolones, including Ciprofloxacin, have been associated with prolongation of the QT interval on the electrocardiogram and cases of arrhythmia. Cases of torsade de pointes have been reported during post marketing surveillance in patients receiving fluoroquinolones. Avoid Ciprofloxacin in patients with known prolongation of the QT interval, risk factors for QT prolongation or torsade de pointes (for example, congenital long QT syndrome, uncorrected electrolyte imbalance, such as hypokalemia or hypomagnesemia and cardiac disease, such as heart failure, myocardial infarction, or bradycardia), and patients receiving Class IA antiarrhythmic agents (quinidine, procainamide), or Class III antiarrhythmic agents (amiodarone, sotalol), tricyclic antidepressants, macrolides, and antipsychotics. Elderly patients may also be more susceptible to drug-associated effects on the QT interval.

Musculoskeletal disorders in pediatric patients and arthropathic effects in animals: Ciprofloxacin is indicated in pediatric patients (less than 18 years of age) only for cUTI, prevention of inhalational anthrax (post exposure), and plague. An increased incidence of adverse reactions compared to controls, including reactions related to joints and/or surrounding tissues, has been observed.

Photosensitivity/Phototoxicity: Moderate to severe photosensitivity/phototoxicity reactions, the latter of which may manifest as exaggerated sunburn reactions (for example, burning, erythema, exudation, vesicles, blistering, edema) involving areas exposed to light (typically the face, “V” area of the neck, extensor surfaces of the forearms, dorsa of the hands), can be associated with the use of quinolones after sun or UV light exposure.

Development of drug resistant bacteria: Prescribing Ciprofloxacin 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.

Potential risks with concomitant use of drugs metabolized by cytochrome p450 1a2 enzymes: Ciprofloxacin is an inhibitor of the hepatic CYP1A2 enzyme pathway. Co-administration of Ciprofloxacin and other drugs primarily metabolized by CYP1A2 (for example, theophylline, methylxanthines, caffeine, tizanidine, ropinirole, clozapine, olanzapine) results in increased plasma concentrations of the co- administered drug and could lead to clinically significant pharmacodynamic adverse reactions of the co- administered drug.

Interference with timely diagnosis of syphilis:
Ciprofloxacin has not been shown to be effective in the treatment of syphilis. Perform a serologic test for syphilis in all patients with gonorrhea at the time of diagnosis. Perform follow-up serologic test for syphilis three months after Ciprofloxacin treatment.

Crystalluria: Crystalluria related to ciprofloxacin has been reported only rarely in humans because human urine is usually acidic. Hydrate patients well to prevent the formation of highly concentrated urine.

USE IN SPECIFIC POPULATIONS:

Pregnancy:
Pregnancy Category C:
There are no adequate and well-controlled studies in pregnant women. Ciprofloxacin should not be used during pregnancy unless the potential benefit justifies the potential risk to both fetus and mother.

Lactation:
Because of the potential risk of serious adverse reactions (including articular damage) 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:
Although effective in clinical trials, Quinolones, including Ciprofloxacin, cause arthropathy in juvenile animals

Geriatric use:
Caution should be used when prescribing Ciprofloxacin to elderly patients especially those on corticosteroids.

Renal impairment:
Some modification of dosage is recommended, particularly for patients with severe renal dysfunction.

Hepatic impairment:
In preliminary studies in patients with stable chronic liver cirrhosis, no significant changes in ciprofloxacin pharmacokinetics have been observed. The pharmacokinetics of ciprofloxacin in patients with acute hepatic insufficiency, have not been studied.

OVERDOSAGE:
In the event of acute overdosage, reversible renal toxicity has been reported in some cases. Empty the stomach by inducing vomiting or by gastric lavage. Observe the patient carefully and give supportive treatment, including monitoring of renal function, urinary pH and acidify if required, to prevent crystalluria and administration of magnesium, aluminum, or calcium containing antacids which can reduce the absorption of ciprofloxacin. Adequate hydration must be maintained. Only a small amount of ciprofloxacin (less than 10%) is removed from the body after hemodialysis or peritoneal dialysis.

INSTRUCTIONS:

- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:
BACTCID Tablet 250 mg : Pack of 1 x 10 tablets.
BACTCID Tablet 500 mg : Pack of 1 x 10 tablets.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

گرمی، دھوپ اور نمی سے بچائیں۔

بچوں کی پہنچ سے دور رکھیں۔

صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

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