

# Ciprofloxacin Hama Pharma (Film-Coated Tablets)

## Ciprofloxacin 250 mg, 500 mg, 750 mg

**SEE WARNING: TENDON EFFECTS AND MYASTHENIA GRAVIS**

**Composition:** Each film-coated tablet of CIPROFLOXACIN Hama Pharma contains: 250 mg, 500 mg, or 750 mg of Ciprofloxacin (as Ciprofloxacin Hydrochloride Monohydrate).

**Excipients:**

Tablet core: Colloidal silicon dioxide, Croscarmellose sodium, Povidone, Magnesium stearate, Microcrystalline cellulose.

Coating: Hypromellose, Titanium dioxide, PEG 6000.

**MECHANISM OF ACTION:** The bactericidal action of Ciprofloxacin results from inhibition of the enzymes topoisomerase II (DNA gyrase) and topoisomerase IV (both Type II topoisomerases), which are required for bacterial DNA replication, transcription, repair, and recombination.

**PHARMACOKINETICS:** The absolute bioavailability of Ciprofloxacin when given as an oral capsule is approximately 70%. Maximum serum concentrations are attained 1 to 2 hours after oral dosing. Ciprofloxacin is an inhibitor of human cytochrome P450 1A2 (CYP1A2) mediated metabolism. 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.

**INDICATIONS:** It is indicated for the treatment of infections caused by susceptible isolates of the designated microorganisms in the conditions and patient populations listed below.

**In Adult Patients:**

1. Urinary Tract Infections caused by *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Serratia marcescens*, *Proteus mirabilis*, *Providencia rettgeri*, *Morganella morganii*, *Citrobacter koseri*, *Citrobacter freundii*, *Pseudomonas aeruginosa*, methicillin-susceptible *Staphylococcus epidermidis*, *Staphylococcus saprophyticus*, or *Enterococcus faecalis*.
2. Acute Uncomplicated Cystitis in Females caused by *Escherichia coli* or *Staphylococcus saprophyticus*.
3. Chronic Bacterial Prostatitis caused by *Escherichia coli* or *Proteus mirabilis*.
4. Lower Respiratory Tract Infections caused by *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, or penicillin-susceptible *Streptococcus pneumoniae* and for the treatment of acute exacerbations of chronic bronchitis caused by *Moraxella catarrhalis*.
5. Acute Sinusitis caused by *Haemophilus influenzae*, *Streptococcus pneumoniae*, or *Moraxella catarrhalis*.
6. 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*, methicillin-susceptible *Staphylococcus aureus*, methicillin-susceptible *Staphylococcus epidermidis*, or *Streptococcus pyogenes*.
7. Bone and Joint Infections caused by *Enterobacter cloacae*, *Serratia marcescens*, or *Pseudomonas aeruginosa*.
8. Complicated Intra-Abdominal Infections (used in combination with metronidazole) caused by *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Klebsiella pneumoniae*, or *Bacteroides fragilis*.
9. Infectious Diarrhea caused by *Escherichia coli* (enterotoxigenic isolates), *Campylobacter jejuni*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri* or *Shigella sonnei* when antibiogram therapy is indicated.
10. Typhoid Fever (Enteric Fever) caused by *Salmonella typhi* (The efficacy of Ciprofloxacin in the eradication of the chronic typhoid carrier state has not been demonstrated).
11. Uncomplicated Cervical and Urethral Gonorrhoea due to *Neisseria gonorrhoeae*.

**In pediatric patients (1 to 17 years of age):**

- Complicated Urinary Tract Infections and Pyelonephritis in one to 17 years of age due to *Escherichia coli*

**Adult and Pediatric Patients (from birth to 17 years of age):**

1. Inhalational Anthrax (post-exposure): To reduce the incidence or progression of disease following exposure to aerosolized *Bacillus anthracis*.
2. Treatment of plague including pneumonic and septicemic plague, due to *Yersinia pestis* and prophylaxis. Efficacy studies of Ciprofloxacin could not be conducted in humans with plague for feasibility reasons. Therefore, this indication is based on an efficacy study conducted in animals only.

**Limitation of Use:**

- Ciprofloxacin film-coated tablets, are not a drug of first choice in the treatment of presumed or confirmed pneumonia secondary to *Streptococcus pneumoniae*.
- 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. Therapy with Ciprofloxacin may be initiated before results of these tests are known; once results become available appropriate therapy should be continued. As with other drugs, some isolates of *Pseudomonas aeruginosa* may develop resistance during treatment with Ciprofloxacin.

**CONTRAINDICATIONS:**

- History of hypersensitivity to ciprofloxacin, any member of the quinolone class or any component of the product.
- Concomitant administration with tizanidine.

**SIDE EFFECTS:** The most frequently reported side effects include nausea, diarrhea, abnormal liver function tests, vomiting and rash.

**WARNINGS & PRECAUTIONS:**

**Tendinopathy and Tendon Rupture:** Fluoroquinolones, including Ciprofloxacin, are associated with an increased risk of tendinitis and tendon rupture in all ages. This risk is increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart, or lung transplants. In addition to age and corticosteroid use, there are factors that may independently increase the risk of tendon rupture include strenuous physical activity, renal failure, and previous tendon disorders such as rheumatoid arthritis. Ciprofloxacin should be used with caution in patients with a history of tendon disorders. Ciprofloxacin should be discontinued if the patient experiences pain, swelling, inflammation or rupture of a tendon. Inflammation and tendon rupture can occur; sometimes bilaterally, even within the first 48 hours, during or after completion of therapy.

**Myasthenia gravis:** Fluoroquinolones, including Ciprofloxacin, may exacerbate muscle weakness in persons with myasthenia gravis. Avoid Ciprofloxacin in patients with known history of myasthenia gravis.

**Hypersensitivity Reactions:** Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving quinolone therapy, including Ciprofloxacin. Serious anaphylactic reactions require immediate emergency treatment. Other serious and sometimes fatal events, some due to hypersensitivity, and some due to uncertain, have been reported in patients receiving therapy with quinolones, including Ciprofloxacin. Discontinue Ciprofloxacin immediately at the first appearance of a skin rash, jaundice, or any other sign of hypersensitivity and supportive measures instituted.

**Hepatotoxicity:** Cases of severe hepatotoxicity, including hepatic necrosis, life-threatening hepatic failure, and fatal events, have been reported with Ciprofloxacin. 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.

**Central Nervous System Effects:** Convulsions, increased intracranial pressure and toxic psychosis have been reported in patients receiving fluoroquinolones, including Ciprofloxacin. Ciprofloxacin may also cause central nervous system (CNS) events. These reactions may occur following the first dose. Advise patients receiving Ciprofloxacin to inform their healthcare provider immediately if CNS events occur, discontinue the drug, and institute appropriate care. Ciprofloxacin, like other fluoroquinolones, is known to trigger seizures or lower the seizure threshold. As with all fluoroquinolones, use Ciprofloxacin with caution in epileptic patients and patients with known or suspected CNS disorders that may predispose to seizures or lower the seizure threshold or in the presence of other risk factors 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. If seizures occur, discontinue Ciprofloxacin.

**Clostridium 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, if it is suspected or confirmed, ongoing antibacterial use not directed against *C. difficile* may need to be discontinued and appropriate management should be instituted.

**Peripheral Neuropathy:** Cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesias, hypoesthesias, dyesthesias and weakness have been reported in patients receiving fluoroquinolones, including Ciprofloxacin. Discontinue Ciprofloxacin immediately if the patient experiences symptoms of peripheral neuropathy in order to minimize the development of an irreversible condition.

**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. Avoid Ciprofloxacin in patients with known prolongation of the QT interval, risk factors for QT prolongation or torsade de pointes, and patients receiving Class IA antiarrhythmic (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.

**Crystalluria:** Crystalluria related to Ciprofloxacin has been reported rarely in humans. Avoid alkalinity of the urine in patients receiving Ciprofloxacin. Hydrate patients well to prevent the formation of highly concentrated urine.

**Photosensitivity/Phototoxicity:** moderate to severe photosensitivity/phototoxicity reactions can be associated with the use of quinolones including Ciprofloxacin after sun or UV light exposure. Therefore, avoid excessive exposure to these sources of light. Discontinue Ciprofloxacin if phototoxicity occurs.

**Resistant:** prescribing Ciprofloxacin film-coated 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. When culture and susceptibility information are available, they should be considered in selecting or modifying antibiogram therapy.

**Interference with Diagnosis of Syphilis:** 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. 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.

**Pregnancy teratogenic effects, 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.

**Nursing Mothers:** Ciprofloxacin is excreted in human milk. The amount of ciprofloxacin absorbed by the nursing infant is unknown. 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:** Although effective in clinical trials, Ciprofloxacin is not a drug of first choice in the pediatric population due to an increased incidence of adverse reactions compared to controls events related to joints and/or surrounding tissues. Quinolones, including Ciprofloxacin, cause arthropathy in juvenile animals.

**Geriatric Use:** 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.

**DRUG INTERACTIONS:**

- Ciprofloxacin should be taken at least two hours before or six hours after Multivalent cation-containing products administration (magnesium/aluminum antacids or sucralate or other products containing calcium, iron or zinc). Concomitant administration of Ciprofloxacin film-coated tablets with dairy products (like milk or yogurt) or calcium-fortified juices alone should be avoided since decreased absorption is possible.

- Ciprofloxacin is an inhibitor of cytochrome P450 1A2 (CYP1A2) mediated metabolism. Co-administration of Ciprofloxacin with other drugs primarily metabolized by CYP1A2 (for example, theophylline, methylxanthines, caffeine, tizanidine, ropinirole, clozapine, olanzapine) results in increased plasma concentrations of these drugs and could lead to clinically significant adverse events of the co-administered drug.

- **Ropinirole:** it is recommended to avoid the concomitant use. Monitoring for ropinirole-related adverse reactions and appropriate dose adjustment of ropinirole is also recommended.

- **Clozapine:** it is recommended to use it with caution. Careful monitoring of clozapine associated adverse reactions and appropriate adjustment of clozapine is advised.

- **Theophylline:** it is recommended to avoid the concomitant use, because it use may result in increased risk of a patient developing CNS or other adverse reactions, if concomitant administration cannot be avoided, serum levels of theophylline should be monitored & dosage adjustment made appropriate.

- **Caffeine, Xanthine Derivatives:** it is recommended to use it with caution, because reduced clearance results in elevated levels and prolongation of serum half-life.

- **Drugs Known to Prolong QT Interval:** Ciprofloxacin may further prolong the QT interval in patients receiving drugs known to prolong the QT interval, it is recommended to avoid the concomitant use.

- **Oral anti diabetic drugs:** Hypoglycemia sometimes severe has been reported with the concomitant use, mainly sulfonylureas. It is recommended to use it with caution because of the Glucose-lowering effect potentiating.

- **Phenytoin:** it is recommended to use it with caution, because of altered serum levels of phenytoin (increased and decreased).

- **Cyclosporine:** it is recommended to use it with caution; because it has been associated with transient elevations serum (renal function should be monitored).

- **Anti-coagulant:** it is recommended to use it with caution, because of increase in the anticoagulant effect.

- **Methotrexate:** it is recommended to use it with caution, because of Potential increase in the risk of methotrexate associated toxic reactions. Therefore, carefully monitoring of the patients is indicated.

- **NSAIDs:** it is recommended to use it with caution, because combination with ciprofloxacin in very high doses of quinolones has been shown to provoke convulsions in preclinical studies.

- **Sildenafil:** it is recommended to use it with caution and monitor for sildenafil toxicity.

- **Duloxetine:** it is recommended to avoid the concomitant use; if it is unavoidable duloxetine toxicity should be monitored.

- **Probenecid:** the concomitant use may result in Potentiation of Ciprofloxacin toxicity, therefore it is recommended to use it with caution.



**DOSAGE AND ADMINISTRATION:**

Adult dosage: Generally Ciprofloxacin should be continued for at least 2 days after the signs and symptoms of infection have disappeared, except for inhalational anthrax.

Infection	Dose	Frequency	Usual Durations
Urinary Tract	250 to 500 mg	every 12 hours	7 to 14 days
Acute Uncomplicated Cystitis	250 mg	every 12 hours	3 days
Chronic Bacterial Prostatitis	500 mg	every 12 hours	28 days
Lower Respiratory Tract	500 to 750 mg	every 12 hours	7 to 14 days
Acute Sinusitis	500 mg	every 12 hours	10 days
Skin and Skin Structure	500 to 750 mg	every 12 hours	7 to 14 days
Bone and Joint	500 to 750 mg	every 12 hours	4 to 8 weeks
Complicated Intra-Abdominal (Used in conjunction with metronidazole)	500 mg	every 12 hours	7 to 14 days
Infectious Diarrhea	500 mg	every 12 hours	5 to 7 days
Typhoid Fever	500 mg	every 12 hours	10 days
Uncomplicated Urethral and Cervical Gonococcal Infections	250 mg	single dose	single dose
Inhalational anthrax (post-exposure)	500 mg	every 12 hours	60 days
Plague	500 to 750 mg	every 12 hours	14 days

Inhalational anthrax (post-exposure) and Plague (Begin drug administration as soon as possible after suspected or confirmed exposure)

**Conversion of IV to Oral Dosing in Adults:**

Patients whose therapy is started with Ciprofloxacin IV may be switched to Ciprofloxacin film-coated tablets when the physician prescribe it:

Ciprofloxacin Oral Dosage	Equivalent Ciprofloxacin IV Dosage
250 mg film-coated tablet every 12 hours	200 mg intravenous every 12 hours
500 mg film-coated tablet every 12 hours	400 mg intravenous every 12 hours
750 mg film-coated tablet every 12 hours	400 mg intravenous every 8 hours

**Dosage in Pediatric Patients:**

Dosing and initial route of therapy (that is, IV or oral) for cUTI or pyelonephritis should be determined by the severity of the infection.

Infection	Dose	Frequency	Total Duration
Complicated Urinary Tract or Pyelonephritis (patients from 1 to 17 years of age)	10 mg/kg to 20 mg/kg (maximum 750 mg per dose; not to be exceeded even in patients weighing more than 51 kg)	Every 12 Hrs	10 to 21 days
Inhalational Anthrax (Post-Exposure)	15 mg/kg (maximum 500 mg per dose)	Every 12 Hrs	60 days
Plague	15 mg/kg (maximum 500 mg per dose)	Every 12 to 8 Hrs	10 to 21 days

The total duration of therapy for cUTI and pyelonephritis in the clinical trial was determined by the physician. The mean duration of treatment was 11 days. Inhalational anthrax (post-exposure) and Plague (Begin drug administration as soon as possible after suspected or confirmed exposure)

**Dosage Modifications in Patients with Renal Impairment:**

Ciprofloxacin is eliminated primarily by renal excretion, some modification of dosage is recommended, particularly for patients with severe renal dysfunction.

Creatinine Clearance (ml/min)	Dose
> 50	See Usual Dosage.
30 to 50	250 to 500 mg every 12 hours
5 to 29	250 to 500 mg every 18 hours

Patients on hemodialysis or Peritoneal dialysis: 250 to 500 mg every 24 hours (after dialysis)

- In patients with severe infections and severe renal impairment, a unit dose of 750 mg may be administered at the intervals noted above. Patients should be carefully monitored.
- No information is available on dosing adjustments necessary for pediatric patients with moderate to severe renal insufficiency.

**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 over dosage, reversible renal toxicity has been reported in some cases. 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 ciprofloxacin. Adequate hydration must be maintained. Only a small amount of ciprofloxacin (< 10%) is removed from the body after hemodialysis or peritoneal dialysis.

**PACKAGING:** 1 or 2 blisters, each contains 10 film-coated tablets/carton box.

**STORAGE CONDITIONS:** Store at room temperature, below 30° C.

Keep out of reach of children.

TPP180000•	<b>THIS IS A MEDICAMENT</b>
– A medicament is a product but unlike any other products. – 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 for you. – Do not repeat the same prescription without consulting your doctor.	
<b>KEEP MEDICAMENTS OUT OF REACH OF CHILDREN</b> (Council of Arab Health Ministers) (Arab Pharmacists Association)	

Manufactured by:  
 HAMA PHARMA Hama - Syria  
 Tel.: +963 33 8673941 Fax: +963 33 8673943



