

Alacep®

(USP Specification)

Ciprofloxacin HCl

(USP Specification)

250mg & 500mg Film Coated Tablets

COMPOSITION

Alacep 250mg Tablets: Each film coated tablet contains:

Ciprofloxacin as Hydrochloride 250mg

(USP Specification)

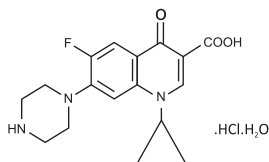
Alacep 500mg Tablets: Each film coated tablet contains:

Ciprofloxacin as Hydrochloride 500mg

(USP Specification)

DESCRIPTION

ALACEP (Ciprofloxacin HCl) is a synthetic carboxyquinolone derivative with broad spectrum antimicrobial activity. It is the monohydrochloride monohydrate salt of 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid. The CAS Registry number is [86393-32-0]. It is a faintly yellowish to yellow crystalline substance with a molecular weight of 385.8. Its empirical formula is $C_{17}H_{18}FN_3O_3 \cdot HCl \cdot H_2O$ and its chemical structure is as follows;



CLINICAL PARTICULARS

Therapeutic Indications:

ALACEP (Ciprofloxacin HCl) is indicated for the treatment of infections caused by susceptible organisms in the conditions listed below:

- Urinary tract infections
- Gonorrhoeal urethritis and cervicitis
- Gastroenteritis
- Bronchial Infections
- Skin and skin structure infections
- Bone and joint infections
- Chronic bacterial prostatitis of mild to moderate severity
- Inhalational anthrax (post-exposure): To reduce the incidence or progression of disease following exposure to aerosolized *Bacillus anthracis*. **ALACEP** (Ciprofloxacin HCl) serum concentrations achieved in humans serve as a surrogate endpoint reasonably likely to predict clinical benefit and provide the basis for this indication.

Dosage and administration:

Urinary tract infections - The usual adult dosage is 250 mg every 12 hours. For patients with complicated infections caused by organisms not highly susceptible, such as *Enterococcus faecalis*, 500 mg may be administered every 12 hours.

Bronchial infections, skin and skin structure infections - The usual dose is 500 mg every 12 hours. For more severe or complicated infections, a dosage of 750 mg may be given every 12 hours.

Bone and joint infections - 750 mg every 12 hours.

Gastroenteritis (infectious diarrhoea) - 500 mg every 12 hours.

Acute, uncomplicated gonorrhoeal urethritis - A single dose of 250 mg.

Chronic bacterial prostatitis - 250 to 500mg every 12 hours.

Inhalational anthrax (post-exposure) - for adults, the recommended dose is 500 mg every 12 hours. For paediatric patients, the recommended dose is 15 mg/kg per dose (not to exceed 500 mg per dose), every 12 hours. Drug administration should begin as soon as possible after suspected or confirmed exposure.

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-defence mechanisms, and the status of renal function.

Because Gram-positive organisms are generally less sensitive than Gram-negative organisms, the use of higher doses should be considered in patients with Gram-positive infections. In such cases 8 hourly administration of 500mg **ALACEP** (Ciprofloxacin HCl) may be preferable.

Duration: The duration of treatment depends upon the severity of infection. Generally **ALACEP** (Ciprofloxacin HCl) 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. Gastrointestinal infections (infectious

diarrhoea) need treatment for only 5 days. Chronic bacterial prostatitis should be treated for 14 to 28 days.

Inhalational anthrax (post exposure) should be treated for 60 days. Drug administration should begin as soon as possible after suspected or confirmed exposure.

In certain deep-seated infections involving abscess formation, appropriate surgical drainage should be performed in conjunction with antimicrobial therapy.

Impaired Renal Function: Dosage adjustments: For patients with creatinine clearance between 31-60 mL/min/1.73m², the maximum daily dose should be 1000 mg/day for oral administration. For creatinine clearance equal or less than 30 mL/min/1.73m², the maximum daily dose should be 500 mg/day for oral administration.

When only data for serum creatinine are available, the following formula (Cockcroft's equation) may be used to estimate creatinine clearance.
Men: Creatinine Clearance (mL/min) = $\{[(\text{Weight in kg}) \times (140 - \text{age})] / (72 \times \text{serum creatinine in mmol/L})\} \times 0.0885$

Women: $0.85 \times$ the value calculated for men

Contraindications:

A history of hypersensitivity to **ALACEP** (Ciprofloxacin HCl) or other quinolones, including nalidixic acid, or any of the excipients.

Concurrent administration of **ALACEP** (Ciprofloxacin HCl) and tizanidine.

Precautions:

ALACEP (Ciprofloxacin HCl) should be used with caution in patients with a history of convulsive disorders. Increased serum levels of theophylline have been observed following concurrent administration of other quinolones.

Drug Interactions:

ALACEP (Ciprofloxacin HCl), like other fluoroquinolones should be used with caution in patients receiving drugs known to prolong the QT interval (e.g. Class IA and III anti-arrhythmics, tricyclic antidepressants, macrolides, antipsychotics).

Concurrent administration of **ALACEP** (Ciprofloxacin HCl) with theophylline may lead to elevated plasma concentrations of theophylline and prolongation of its elimination half-life. This can lead to theophylline-induced side effects; in very rare cases these side effects can be life threatening or fatal. If concomitant use cannot be avoided, the plasma levels of theophylline should be monitored and appropriate dosage adjustments should be made.

Concomitant administration of **ALACEP** (Ciprofloxacin HCl) and omeprazole results in a slight reduction of C_{max} and AUC of **ALACEP** (Ciprofloxacin HCl).

Hypoglycaemia has been reported when **ALACEP** (Ciprofloxacin HCl) and oral antidiabetic agents, mainly sulfonylureas (e.g. glibenclamide, glibenipride), where co-administered, presumably by intensifying the action of the oral antidiabetic agent.

Animal studies have shown that the combination of very high doses of quinolones (gyrase inhibitors) and certain non-steroidal anti-inflammatory agents (but not acetylsalicylic acid) can provoke convulsions.

Pregnancy:

Pregnancy Category B3: Reproduction studies have been performed in rats and mice at doses up to 100 mg/kg (0.6 and 0.3 times the maximum daily human dose based upon body surface area, respectively) and IV doses of up to 30 mg/kg and have revealed no evidence of impaired fertility or harm to the fetus due to **ALACEP** (Ciprofloxacin HCl). In rabbits, **ALACEP** (Ciprofloxacin HCl) (30 and 100 mg/kg orally, 0.4 and 1.2 times the maximum daily human dose based upon body surface area, respectively) produced gastrointestinal disturbances resulting in maternal weight loss and an increased incidence of abortion, intra-uterine deaths and fetal retardation, but no teratogenicity was observed at either dose. After intravenous administration, at doses up to 20 mg/kg, no maternal toxicity was produced in the rabbit and no embryotoxicity or teratogenicity was observed. There are, however, no adequate and well-controlled studies in pregnant women.

Like other drugs in its class, **ALACEP** (Ciprofloxacin HCl) causes arthropathy in immature animals. **ALACEP** (Ciprofloxacin HCl) should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus. (e.g. potential damage to articular cartilage in the immature fetal organism).

Lactation:

ALACEP (Ciprofloxacin HCl) is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from **ALACEP** (Ciprofloxacin HCl), a decision should be made to discontinue nursing or to avoid using the drug, taking into account the importance of the drug to the mother.

Geriatric Use:

ALACEP (Ciprofloxacin HCl) should be used with caution in the elderly after taking into account the severity of the illness and the creatinine clearance.

Adverse Reactions:

The following adverse effects have been observed:

Effects on the gastrointestinal tract: Nausea, diarrhoea, vomiting, digestive disorders, abdominal pain, flatulence and anorexia may occur. The doctor should be advised of any severe or persistent diarrhoea occurring during or after treatment since these symptoms could conceal a serious intestinal disorder (pseudo-membranous colitis) requiring urgent treatment. In such cases, **ALACEP** (Ciprofloxacin HCl) should be discontinued and replaced by another appropriate drug (e.g., vancomycin orally, 4 x 250 mg/day). Preparations which inhibit peristalsis are contraindicated.

Effects on the nervous system: Dizziness, headache, tiredness, insomnia, agitation, trembling; very rarely peripheral paralgesia, sweating, unsteady gait, convulsions, anxiety states, nightmares, confusion, depression, hallucinations, impaired taste and smell, visual disturbances (e.g., double vision, color vision). In some instances, these reactions occur after the first administration of **ALACEP** (Ciprofloxacin HCl). In these cases **ALACEP** (Ciprofloxacin HCl) has to be discontinued and the doctor should be informed immediately.

Hypersensitivity Reactions: Skin reactions, e.g., rashes, pruritus, urticaria, photosensitivity. Systemic reactions including anaphylaxis.

Effects on Cardiovascular System: Very rarely tachycardia, hot flushes, migraine & fainting.

Effects on laboratory values/urine deposits: There may be a transient rise in the transaminase and alkaline phosphate levels or cholestatic jaundice may occur, particularly in patients with previous liver damage; transient increase in serum urea, creatinine and bilirubin levels, hyperglycaemia; in individual cases: crystalluria and haematuria.

Effects on the total blood picture: Eosinophilia, leucocytopenia, leucocytosis, anaemia; very rarely: thrombocytopenia, thrombocytosis, altered prothrombin levels.

CLINICAL PHARMACOLOGY

Pharmacological actions (Microbiology)

ALACEP (Ciprofloxacin HCl) has in vitro activity against a wide range of Gram-negative and Gram-positive organisms. The bactericidal action of **ALACEP** (Ciprofloxacin HCl) appears to result from interference with the enzyme, DNA gyrase. **ALACEP** (Ciprofloxacin HCl) is usually active against the following organisms in vitro.

Gram-Negative: Escherichia coli; Klebsiella species (including Klebsiella pneumoniae and Klebsiella oxytoca); Enterobacter species; Citrobacter species; Salmonella species; Shigella species; Proteus mirabilis; Proteus vulgaris; Providencia stuartii; Providencia rettgeri (formerly Proteus rettgeri); Morganella morganii (formerly Proteus morganii); Serratia species* (including Serratia marcescens); Pseudomonas aeruginosa; Pseudomonas fluorescens; Campylobacter species; Haemophilus influenzae; Moraxella (Branhamella) catarrhalis.

Gram-Positive: Staphylococcus aureus (including methicillin-susceptible and methicillin-resistant strains); coagulase negative Staphylococcus species (including Staphylococcus epidermidis); Streptococcus pyogenes (group A); Streptococcus pneumoniae; Enterococcus faecalis.

Pharmacokinetics:

Absorption:

ALACEP (Ciprofloxacin HCl) tablets are rapidly and well absorbed from the gastrointestinal tract after oral administration. The absolute bioavailability is approximately 70% with no substantial loss by first pass metabolism. Co-administration of **ALACEP** (Ciprofloxacin HCl) with food appears to lower peak serum levels and delays the absorption of **ALACEP** (Ciprofloxacin HCl), resulting in peak concentrations closer to 2 hours after dosing rather than 1 hour. The overall absorption, however, is not substantially affected. Absorption also appears to be greatly reduced by prior administration of antacids.

Distribution: After oral dosing, **ALACEP** (Ciprofloxacin HCl) is widely distributed throughout the body. The binding of **ALACEP** (Ciprofloxacin HCl) to serum proteins is 20 to 40%. Serum concentrations increase in a dose proportional manner and were, after multiple doses, as shown below:

Dose (mg)	Maximum Serum Concentration (µg/mL)	Area Under Curve (AUC) (µg.hr/mL)
250	1.4	5.4
500	2.6	10.6
750	3.4	15.0

Maximum serum concentrations are attained 1 to 2 hours after oral dosing. Mean concentrations 12 hours after dosing with 250, 500 or 750 mg are 0.1, 0.2 and 0.4 µg/mL respectively.

Metabolism: **ALACEP** (Ciprofloxacin HCl) is also metabolized. Four metabolites have been identified in human urine which together account for approximately 15% of an oral dose. The metabolites have less antimicrobial activity than unchanged **ALACEP** (Ciprofloxacin HCl).

Elimination: 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. During the first 2 hours after an oral dose of 250 mg, the urine concentration of **ALACEP** (Ciprofloxacin HCl) usually exceeds 200 µg/mL. Eight to 12 hours after the same dose, urine levels are approximately 30 µg/mL. Urinary excretion of **ALACEP** (Ciprofloxacin HCl) is virtually completed within 24 hours after

dosing. The renal clearance of **ALACEP** (Ciprofloxacin HCl) is approximately 18 L/h which exceeds the normal glomerular filtration rate of 7.2 L/h. Thus, active tubular secretion would seem to play a significant role in its elimination. In patients with creatinine clearance between 21-40 mL/min, the half-life of **ALACEP** (Ciprofloxacin HCl) is only slightly prolonged. Dosage adjustments are usually not required in such cases. However, in patients with severe renal impairment, with creatinine clearance less than 20 mL/min, the half-life of **ALACEP** (Ciprofloxacin HCl) is nearly doubled and dosage adjustment is necessary.

Although bile concentrations of **ALACEP** (Ciprofloxacin HCl) are 3 - 4 times higher than serum concentrations after oral dosing, only a small amount of the dose administered is recovered from the bile. Approximately 20 to 35% of an oral dose is recovered from the faeces within 5 days after dosing.

OVERDOSAGE

In the event of acute, excessive oral overdosage, reversible renal toxicity has been reported in some cases. Therefore, apart from routine emergency measures, it is recommended to monitor renal function, including urinary pH and acidify if required to prevent crystalluria. Patients should be kept well hydrated - Calcium or magnesium containing antacids reduce the absorption of **ALACEP** (Ciprofloxacin HCl) in overdoses.

Only a small quantity of **ALACEP** (Ciprofloxacin HCl) (<10%) is eliminated from the body after haemodialysis or peritoneal dialysis.

STORAGE:

Store at 20-25°C. Protect from light and moisture.
(excursions permitted to 15°C to 30°C)

HOW SUPPLIED

ALACEP 250mg Tablets: Pack of 10 film coated tablets.

ALACEP 500mg Tablets: Pack of 10 film coated tablets.

TO BE SOLD ON THE PRESCRIPTION OF A REGISTERED MEDICAL PRACTITIONER ONLY.

KEEP ALL MEDICINES OUT OF THE REACH OF CHILDREN.

Lactose & Gluten Free

ایلا سیپ

(سپر فلوکساسین ہائیڈروکلورائیڈ)

250 ملی گرام اور 500 ملی گرام

فلم کوئڈ گولیاں

خوراک و ہدایات

ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔

صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت کی جائے۔

تمام ادویات بچوں کی پہنچ سے دور رکھیں۔

دوا کو 20°C-25°C درجہ حرارت پر رکھیں اور روشنی سے محفوظ رکھیں۔

(درجہ حرارت کی حد 15°C سے 30°C ہے)

INEXIT
PHARMACEUTICAL

Manufactured by:
NEXT Pharmaceutical Products (Pvt.) Ltd.
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