CIROK Tablets

Ciprofloxacin 250mg, 500mg

COMPOSITION
Each tablet contains
Ciprofloxacin hydrochloride ..... 291 mg
(As ciprofloxacin 250 mg)
Ciprofloxacin hydrochloride ..... 582 mg
(As ciprofloxacin 500 mg)

DESCRIPTION
White, round film-coated tablets.

INDICATIONS
CIROK is indicated for the treatment of infections.
Treatment of infections caused by the following microorganism; Escherichia coli, Shigella, Salmonella, Citrobacter, Klebsiella, Enterobacter, Serratia, Hafnia Proteus (Indole Positive and negative), Pseudomonas, Neisseria, Acinetobacter, Streptococcus, Clamydia, Staphylococcus, Corynebacterium, Clostridium, Bacteroides.
Infections: Respiratory infections; ear, nose and throat infections; mouth, tooth, genial inflammation, renal or urinary tract infections, genital infections including gonorrhea; gastrointestinal infections, biliation canal infections; bone and joint infections, soft tissue infections; gynecological and obstetrical infections, septicemia, meningitis, peritonitis, ophthalmic infections.

1. DOSAGE AND ADMINISTRATION
The usual adult oral dosage of Ciprofloxacin hydrochloride (CIROK) for mild to moderate infections is 250 ~500 mg, twice a day. For more severe or complicated infections, a dosage of 750 mg may be given twice a day. For the treatment of acute infections, the usual duration is 5 to 10 days. Generally ciprofloxacin should be continued for at least 3 days after the signs and symptoms of infection have disappeared.

2. Impaired Renal Function
The following table provides dosage guidelines for use in patients with impaired renal function: monitoring of serum drug levels provides the most reliable basis for dosage adjustment.

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)

When only the serum creatinine concentration is known, the following formula may be used to estimate creatinine clearance.

- Men :

$$\text{Creatinine Clearance (mL/min)} = \frac{\text{Weight(kg)} \times (140\text{-age})}{72 \times \text{Serum creatinine (mg/dL)}}$$

- Women : 0.85 X the value calculated for men.

In patients with severe infections and severe renal impairment, a unit 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 mcg/mL.
3. The determination of dosage for any particular patient must take into consideration the severity and nature of the infection.

WARNINGS
It has been reported that tendon ruptures of Achilles tendon, shoulders, hands which cause disability or require a surgery. If a patient feels a pain, inflammation, tendon rupture, the administration should be discontinued. And the patient should be take a rest, avoid exercising until it is certained that the symptom is proven not to be a tendinitis or tendon rupture.
Cardiac disorders: Caution should be taken when using fluoroquinolones, including ciprofloxacin, in patients with known risk factors for prolongation of the QT interval such as, for example:
- Congenital long QT syndrome.
- Concomitant use of drugs that are known to prolong the QT interval (e.g. Class IA and III anti-arrhythmics, tricyclic antidepressants, macrolides, antipsychotics).
- Uncorrected electrolyte imbalance(e.g. hypokalaemia, hypomagnesaemia).
- Elderly.
- Cardiac disease (e.g. heart failure, myocardial infarction, bradycardia).

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, including CIROK. Symptoms may occur soon after initiation of CIROK and may be irreversible. CIROK should be discontinued immediately if the patient experiences symptoms of peripheral neuropathy including pain, burning, tingling, numbness, and/or weakness or other alterations of sensation including light touch, pain, temperature, position sense, and vibratory sensation.

Vision disorders
If vision becomes impaired or any effects on the eyes are experienced, an eye specialist should be consulted immediately.

Disabling and potentially irreversible serious adverse reactions
Fluoroquinolones, including CIROK, have been associated with disabling and potentially irreversible serious adverse reactions from different body systems that can occur together in the same patient. Commonly seen adverse reactions include tendinitis, tendon rupture, arthralgia, myalgia, peripheral neuropathy, and central nervous system effects (hallucinations, anxiety, depression, insomnia, severe headaches, and confusion). Patients of any age or without pre-existing risk factors have experienced these adverse reactions.

Discontinue CIROK immediately at the first signs or symptoms of any serious adverse reaction. In addition, avoid the use of fluoroquinolones, including CIROK, in patients who have experienced any of these serious adverse reactions associated with fluoroquinolones.

Aortic aneurysm or dissection
Epidemiologic studies report an increased risk of aortic aneurysm and dissection after intake of fluoroquinolones, particularly in the older population. Therefore, fluoroquinolones should only be used after careful benefit-risk assessment and after consideration of other therapeutic options in patients with positive family history of aneurysm disease, or in patients diagnosed with pre-existing aortic aneurysm and/or aortic dissection, or in presence of other risk factors or conditions predisposing for aortic aneurysm and dissection (e.g. Marfan syndrome, vascular Ehlers-Danlos syndrome, Takayasu arteritis, giant cell arteritis, Behcet's disease, hypertension, known atherosclerosis). In case of sudden abdominal, chest or back pain, patients should be advised to immediately consult a physician in an emergency department.

Psychiatric Adverse Reactions
Fluoroquinolones, including CIROK, have been associated with an increased risk of psychiatric adverse reactions, including: toxic psychosis, hallucinations, or paranoia; depression or suicidal thoughts or acts; anxiety, agitation, or nervousness; confusion, delirium, disorientation, or disturbances in attention; insomnia or nightmares; memory impairment. These adverse reactions may occur following the first dose. If these reactions occur in patients receiving CIROK, discontinue CIROK immediately and institute appropriate measures.

Blood Glucose Disturbances
As with all fluoroquinolones, disturbances in blood glucose, including both hypoglycaemia and hyperglycaemia have been reported with CIROK. In CIROK-treated patients, dysglycaemia occurred predominantly in elderly diabetic patients receiving concomitant treatment with an oral hypoglycaemic agent (for example, sulfonylurea) or with insulin. Severe cases of hypoglycaemia resulting in coma or death have been reported. In diabetic patients, careful monitoring of blood glucose is recommended. If a hypoglycaemic reaction occurs, discontinue CIROK and initiate appropriate therapy Immediately.

Aortic aneurysm or dissection and heart valve regurgitation/incompetence
Epidemiologic studies report an increased risk of aortic aneurysm and dissection, particularly in elderly patients, and of aortic and mitral valve regurgitation after intake of fluoroquinolones. Cases of aortic aneurysm and dissection, sometimes complicated by rupture (including fatal ones), and of regurgitation/incompetence of any of the heart valves have been reported in patients receiving fluoroquinolones.

Therefore, fluoroquinolones should only be used after a careful benefit-risk assessment and after consideration of other therapeutic options in patients with positive family history of aneurysm disease or congenital heart valve disease, or in patients diagnosed with pre-existing aortic aneurysm and/or dissection or heart valve disease, or in presence of other risk factors or conditions predisposing

- for both aortic aneurysm and dissection and heart valve regurgitation/incompetence (e.g. connective tissue disorders such as Marfan syndrome or Ehlers-Danlos syndrome, Turner syndrome, Behçet´s disease, hypertension, rheumatoid arthritis) or additionally
- for aortic aneurysm and dissection (e.g. vascular disorders such as Takayasu arteritis or giant cell arteritis, or known atherosclerosis, or Sjögren's syndrome) or additionally
- for heart valve regurgitation/incompetence (e.g. infective endocarditis).

The risk of aortic aneurysm and dissection, and their rupture may also be increased in patients treated concurrently with systemic corticosteroids.

In case of sudden abdominal, chest or back pain, patients should be advised to immediately consult a physician in an emergency department.

Patients should be advised to seek immediate medical attention in case of acute dyspnoea, new onset of heart palpitations, or development of oedema of the abdomen or lower extremities.

2. The drug is contraindicated in the following patient
Patients with a history of hypersensitivity to ciprofloxacin.
Pregnant women and nursing mothers.
Infants and children.
Patients with epilepsy.
Patients who have a history of rupture and inflammation of tendon, hypersensitivity related to quinolone antibacterials.

3. The administration of the drug should be cautioned
Patients with severe impairment of renal function.
In patients who occurred cerebral seizure, the use of ciprofloxacin should be instituted after appropriate anticonvulsant therapy.
The aged.
Patients with cerebral hemokinetic disorder.
Patients with impaired vein system.

ADVERSE EFFECTIONS
Shock: Rarely, shock may occur, it should therefore observed sufficiently. If any symptom occurs, the administration should be discontinued and appropriate therapy instituted.
Skin: Rarely, muco-cutaneous-ocular syndrome (Stevens-Johnson syndrome), photosensitivity may occur, it should therefore observed sufficiently. If they occur the administration should be discontinued.
Hypersensitivity: Rare cases of pharyngeal edema, facial edema, pruritus, flush, and occasionally, rubor may occur. If they occur the administration should be discontinued.
Renal: Rarely, acute kidney failure, and occasionally, increased serum creatinine and BUN concentration may occur.
Hepatic: Rarely, jaundice, and occasionally, elevations in GOT, GPT, ALP may occur, it should therefore observed sufficiently. If any symptom occurs, the administration should be discontinued and appropriate therapy instituted.
Hematologic: Occasionally, leukopenia, thrombocytopenia, eosinophilia, and rarely, decreased platelet count, oilgochromemia, decreased hematocrit level may occur.
Digestive system: Rarely, severe colitis accompanied with hemafecia, including pseudomembraneous colitis, may occur. If abdominal pain, frequent diarrhea occur, an appropriate therapy, such as discontinuation of the therapy, should be instituted. Occasionally, anorexia, diarrhea, gastric discomfort, vomiturition, vomiting, abdominal pain, abdominal distention, and rarely, stomatitis may also occur.
Central nervous system: Occasionally, headache, dizziness, and rarely, lingual numbness, drowsiness, tremor, visual disorder may occur.
Muscle: Myalgia, a sense of exhaustion, increased CPK, myocytosis of striated muscle accompanied with sudden ingravescence of renal function, which increases myoglobin in blood and urine may occur, it should therefore be cautioned.
Respiratory system: Interstitial pneumonia, accompanied with flush, bex, dyspnea, disorder of chest X-ray, eosinophilia, may occur. If these symptoms occur, the administration should be discontinued and appropriate therapy, including adenocortical hormone therapy, instituted.
Cardiac disorder: Not known: ventricular arrhythmia and torsades de pointes (reported predominantly in patients with risk factors for QT prolongation), ECG QT prolonged.
Nervous system disorders (frequency not known): Peripheral neuropathy (that may be irreversible) and polyneuropathy.
Other: 1. Rarely, arthralgia may occur. 2. Rare case of hypoglycemia by other new quinolone antibacterials has been reported (it occurs frequently in the elderly patients, especially, patients with renal impairment), it should therefore cautioned. 3. Seizure, somnipathy may occur.

4. DRUG INTERACTIONS
1. Concomitant administration of CIROK in patients receiving a theophylline may result in higher and prolonged serum theophylline concentrations. If plasma theophylline concentrations are increased, concomitant use of CIROK and a theophylline should be avoided if possible.
2. Concomitant use of CIROK with ketoprofen may cause convulsion rarely, it should therefore be avoided. Concomitant use of CIROK with other phenylacetic acid group or propionic acid group anti-inflammatory agents (NSAID) may also cause convulsion, it should therefore be taken with caution.
3. Concurrent administration of CIROK with antacids containing magnesium, aluminum, or calcium with sucralfate or divalent and trivalent cations such as iron may substantially interfere with the absorption of CIROK, resulting in serum and urine levels considerably lower than desired.
4. CIROK is associated with transient elevations in serum creatinine in patients receiving cyclosphorine concomitantly.
5. Drugs known to prolong QT interval: Ciprofloxacin, 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).

5. USE TO PREGNANCY AND NURSING MOTHERS
Safety use during pregnancy and lactation has not been established and it should not therefore administered.

6. USE TO CHILDREN
Safety use in children has not been established and therefore its use in children is not recommended.

7. General precautions
1) Patients with disposition should be receive counselling with respect of adverse effects, including seizure or other CNS effects.
2) If pain, inflammatory, tendon rupture occur, the administration should be discontinued, and the patients consult with a physician, and take a rest until it is certained that the symtom is proven not to be a tendinitis or tendon rupture.

OVERDOSE
In the event of overdose, symptomatic treatment should be implemented. ECG monitoring should be undertaken, because of possibility of QT interval prolongation.

OTHERS
In a foreign country, rare cases of tendon disorder, such as Achilles tendinitis, tendon rupture, have been

reported, it should therefore observed sufficiently. If any symptom occurs, the administration should be discontinued and appropriate therapy instituted.
In animal studies (young dogs, young rats), dysarthrosis has been occurred.
In mass-dose administration (more than 750mg/time), crystalluria has been reported.

STORAGE
Store in cool and dry places.

PACKAGE
10, 50, 100, 500, 1000 tablets.

REG. NO. : SIN 11575P (Cirok Tab. 250 mg)
REG. NO. : SIN 11576P (Cirok Tab. 500 mg)

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