CIROK Inj.

Ciprofloxacin 2mg/mL

COMPOSITION
Each mL contains
Ciprofloxacin ……..2 mg

DESCRIPTION
Clear, colorless to pale yellow solution in a vial.

INDICATIONS
CIROK is indicated for the treatment of the following infections caused by sensitive bacteria. Severe systemic infections eg septicemia. Respiratory tract infection eg pneumonia. Urinary tract infection. Skin and soft tissue infections. Intra-abdominal infection. Bone and joint infection.

DOSAGE AND ADMINISTRATIONS
General dosage recommendeds : The dosage of ciprofloxacin is determined by the severity and type of infection, the sensitivity of the causative organism(s) and the age, weight and renal function of the patient.
The recommended adult dosage for urinary tract infections of mild to moderate severity is 200 mg every 12 hours. For severe or complicated urinary tract infections the recommended dosage is 400 mg every 12 hours.
The recommended adult dosage for lower respiratory tract infections, skin and skin structure infections and bone and joint infections of mild to moderate severity is 400 mg every 12 hours.
The usual duration is 7 to 14 days. Bone and joint infections may require treatment for 4 to 6 weeks or longer. And should be treated for at least 2 days after the signs and symptoms of the infection have disappeared.
CIROK should be administered by intravenous infusion over a period 60 minutes.
Impaired Renal function :
The following table provides dosage guidelines for use in patients with renal impairment : monitoring of serum drug level provides the most reliable basis for dosage adjustment.

Creatinine Clearance (mL/min)	Dosage
≥ 30	See usual dosage
5 - 29	200 – 400 mg q 18 – 24 hr

When only the serum creatinine concentration is known, the following formula may be used to estimate creatinine clearance.
- Men : Creatinine Clearance

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

- Women : 0.85 × the value calculated for men.
Initial intravenous administration may be following by treatment with oral ciprofloxacin.

WARNINGS
It has been reported that tendon ruptures of achilles tendon, shoulders, hands which cause disability require a surgery. If a patient feels a pain, inflammation, tendon rupture, the administration should be discontinued. And the patient should take a rest, avoid exercising until it is certain that the symptoms are proven not to be a tendonitis 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).

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.

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

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.

CONTRAINDICATIONS
Patients with a history of hypersensitivity to ciprofloxacin.
Pregnant women and nursing mothers.
Infant and children, Patients with epilepsy
Patients who have a history of rupture and inflammation of tendon, hypersensitivity related to quinolone antibacterials.

CAUTIONS
Patients with severe impairment of renal function.
In patients who had 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 REACTIONS
Shock: Rarely, shock may occur and should be observed sufficiently. If any symptoms 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. Discontinue administration if symptoms occur.
Hypersensitivity: Rare cases of pharyngeal edema, facial edema, pruritus, flush, and occasionally, rubor may occur. Discontinue administration if symptoms occur.
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. Discontinue administration if symptoms occur.
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 taken with caution.
Respiratory system: Interstitial pneumonia, accompanied with flush, bex, dyspnea, disorder of chest X, 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: Rarely, arthralgia may occur. 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 be taken with caution.
Seizure, somniopathy may occur.

General Precautions
Patients with disposition should receive counseling with respect to adverse effects, including seizure or other CNS effects.
If pain, inflammatory, tendon ruptures occur, the administration should be discontinued, and the patients should consult with a physician, and take a rest until it is certain that the symptom is proven not to be a tendonitis or tendon rupture

DRUG INTERACTIONS
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.
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.

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.
CIROK is associated with transient elevations in serum creatinine in patients receiving cyclosphorine concomitantly.
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).

USE TO PREGNANCY AND A NURSING MOTHER
Safety use during pregnancy and lactation has not been established and it should not be administered.

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

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

STORAGE
Preserve in sealed containers protected from light.
Store at room temperature.

PACKAGE
100 mg/50 mL : 1, 5, 10, 50 vial(s)
200 mg/100 mL : 1, 5, 10, 50 vial(s)

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