OFCIN F. C. TABLET

Ingredient(s):
Ofcin F. C. Tablet 200mg:
Each oral tablet contains:
Ofloxacin 200mg
Ofcin F. C. Tablet 400mg:
Each oral tablet contains:
Ofloxacin 400mg

Pharmacology (Summary of Pharmacodynamic and Pharmacokinetics):
1. Ofloxacin is bactericidal in action by inhibiting DNA gyrase, an enzyme necessary for bacterial DNA replication, in susceptible organisms. It is active *in vitro* against many Gram-positive aerobic bacteria, including penicillinase producing, non-penicillinase producing, and some methicilin resistant staphylococci. It is also active *in vitro* against most Gram negative aerobic bacteria, including *Enterobacteriaceae* and *Pseudomonas aeruginosa*. It also has some activities *in vitro* against *Chlamydia, Mycoplasma, Mycobacterium*.
2. Ofloxacin is rapidly and almost completely absorbed from the GI tract following oral administration. Peak serum concentrations are generally attained within 0.5 to 2 hours. It is widely distributed into body tissues and fluids following oral administration. Almost 80% of ofloxacin is excreted unchanged in urine and a small percentage of the dose is excreted in urine as metabolites and in feces. In healthy adults with normal renal function, its elimination half-life in the terminal phases averages 4 to 6 hours, although renal impairment will increase its serum concentrations and prolong its half- life.
3. Ofloxacin has some activities against Gram positive and Gram negative anaerobic bacteria; however, high concentrations of the drug generally are required for *in vitro* inhibition and most of these organisms are considered resistant to the drug. This includes *Clostridium* and *Bacteroides* groups.

Indication(s):
For the treatment of infections caused by susceptible strains of microorganism in infections of the urinary tract, lower respiratory tract, skin and soft tissue, gonorrhoea and non-gonococcal urethritis and cervicitis.

Dosage and Administration:
1. Urinary tract infections: 200 to 400mg daily, preferably in the morning, increased if necessary in upper urinary tract infections to 400mg twice daily.
2. Lower respiratory tract infections: 400mg daily, preferably in the morning, increased if necessary to 400mg twice daily.
3. Skin and soft tissue infections: 200 to 400mg twice daily.
4. Uncomplicated gonorrhoea: 400mg as a single dose.
5. Non-gonococcal urethritis and cervicitis: 400mg daily in single or divided doses.
6. Renal impairment: When creatinine clearance is 20 – 50mL/minute, the dosage should be reduced by half (100-200mg). If creatinine clearance is less than 20mL/minute, 100mg should be given every 24 hours. In patients undergoing haemodialysis or peritoneal dialysis, 100mg should be given every 24 hours.
7. Liver impairment: Dose of ofloxacin should be reduced accordingly in patients with impaired liver function.

Contraindication(s):
1. Patient who has shown previous hypersensitivity to this drug or to other quinolone antibiotics.
2. Ofloxacin is contraindicated in patients with a history of epilepsy or with a lowered seizure threshold.
3. Ofloxacin is contraindicated in children or growing adolescents and in pregnant or breast-feeding women.

Precaution(s) / Warning(s):
1. Patients on ofloxacin should be cautioned to avoid excessive exposure to direct sunlight while receiving the drug. If photosensitivity occurs (e.g. skin eruption), the drug should be discontinued.
2. As with other antibiotics, use of ofloxacin may result in overgrowth of nonsusceptible organisms, especially *enterococci* or *Candida*, Resistant strains of some organisms (e.g. *Pseudomonas aeruginosa, staphylococci*) have developed during ofloxacin therapy. Careful monitoring of the patient and periodic *in vitro* susceptibility tests are essential. If superinfection occurs, appropriate therapy should be instituted.
3. Ofloxacin should be used with caution in patients with renal or hepatic impairment because elimination of the drug is reduced in these patients.
4. Adverse effects may affect performance of skilled tasks (e.g. driving or handling machinery).
5. Dosage of ofloxacin does not need to be modified in geriatric patients with creatinine clearances greater than 50mL/minute.
6. The risk of developing fluoroquinolone-associated tendonitis and tendon rupture is further increased in people older than 60, in those taking corticosteroid drugs, and in kidney, heart and lung transplant recipients. Patients experiencing pain, swelling, inflammation of a tendon or tendon rupture should be advised to stop taking their Ofloxacin medication and to contact their health care professional promptly about changing their antimicrobial therapy. Patients should also avoid exercise and using the affected area of the first sign of tendon pain, swelling, or inflammation.
7. Periodic assessment of organ system function, such as renal, hepatic and hematopoietic, is advisable during prolonged therapy.
8. Adequate hydration of patients receiving ofloxacin should be maintained to prevent the formation of highly concentrated urine.
9. Cardiac disorders:
   Caution should be taken when using fluoroquinolones, including ofloxacin, 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)
10. Exacerbation of Myasthenia Gravis:
    Fluoroquinolones, including ofloxacin, have neuromuscular blocking activity and may exacerbate muscle weakness in persons with myasthenia gravis. Post-marketing serious adverse events, including deaths and requirement for ventilatory support, have been associated with fluoroquinolone use in persons with myasthenia gravis. Avoid ofloxacin in patients with a known history of myasthenia gravis.
11. 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 ofloxacin. Symptoms may occur soon after initiation of Ofcin Film Coated Tablet and may be irreversible. Ofcin Film Coated Tablet 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.
12. Vision Disorder:
    If vision becomes impaired or any effects on the eyes are experienced, an eye specialist should be consulted immediately.
13. Disabling and potentially irreversible serious adverse reactions:
    Fluoroquinolones, including ofloxacin, 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 ofloxacin immediately at the first signs or symptoms of any serious adverse reaction. In addition, avoid the use of fluoroquinolones, including ofloxacin, in patients who have experienced any of these serious adverse reactions associated with fluoroquinolones.
14. 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, Behcet´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.
15. Psychiatric Adverse Reactions:
    Fluoroquinolones, including ofloxacin, 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 ofloxacin, discontinue ofloxacin immediately and institute appropriate measures.
16. Blood Glucose Disturbances:
    As with all fluoroquinolones, disturbances in blood glucose, including both hypoglycaemia and hyperglycaemia have been reported with ofloxacin. In ofloxacin-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 ofloxacin and initiate appropriate therapy immediately.

Drug Interactions:
Drugs known to prolong QT interval
Ofloxacin, 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).

Antacids, Sucralfate, Metal Cations
Co-administered magnesium/aluminium antacids, sucralfate, zinc or iron preparations can reduce absorption. Therefore, ofloxacin should be taken 2 hours before such preparations.

Anticoagulants
Prolongation of bleeding time has been reported during concomitant administration of ofloxacin and anticoagulants.
Coagulation tests should be monitored in patients treated with vitamin K antagonists because of a possible increase in the effect of coumarin derivatives.

Lowering of Seizure Threshold
There may be a further lowering of the cerebral seizure threshold when quinolones are given concurrently with other drugs which lower the seizure

threshold, e.g. theophylline. However ofloxacin is not thought to cause a pharmacokinetic interaction with theophylline, unlike some other fluoroquinolones. Further lowering of the cerebral seizure threshold may also occur with certain nonsteroidal anti-inflammatory drugs.
In case of convulsive seizures, treatment with ofloxacin should be discontinued.

Oral Antidiabetics
Ofloxacin may cause a slight increase in serum concentrations of glibenclamide administered concurrently; patients treated with this combination should be closely monitored.

Renal Tubular Secretion
With high doses of quinolones, impairment of excretion and an increase in serum levels may occur when co-administered with other drugs that undergo renal tubular secretion (e.g. probenecid, cimetidine, furosemide and methotrexate).

Interaction with laboratory tests
Determination of opiates or porphyrins in urine may give false-positive results during treatment with ofloxacin. It may be necessary to confirm positive opiate or porphyrin screens by more specific methods.

Side Effect(s) / Adverse Reaction(s):

System organ class	*Common (≥1/100 to <1/10)*	*Uncommon (≥1/1,000 to <1/100)*	*Rare (≥1/10,000 to <1/1,000)*	*Very rare (<1/10,000)*	*Not known*
Infections and infestations		Fungal infection, Pathogen resistance			
Blood and the lymphatic system disorders				Anaemia, Haemolytic anaemia, Leukopenia, Eosinophilia, Thrombocytopenia	Agranulocytosis, Bone marrow failure
Immune system disorders			Anaphylactic reaction, Anaphylactoid reaction, Angioedema	Anaphylactic shock, Anaphylactoid shock	
Metabolism and nutrition disorders			Anorexia		Hypoglycaemia in diabetics treated with hypoglycaemic agents
Psychiatric disorders		Agitation, Sleep disorder, Insomnia	Psychotic disorder (e.g. hallucination), Anxiety, Confusional state, Nightmares, Depression		Psychotic disorder and depression with self-endangering behaviour including suicidal ideation or suicide attempt
Nervous system disorders		Dizziness, Headache	Somnolence, Paraesthesia, Dysgeusia, Parosmia		Peripheral neuropathy (that may be irreversible) and polyneuropathy
Eye disorders		Eye irritation	Visual disturbance		
Ear and labyrinth disorders		Vertigo		Tinnitus, Hearing loss	
Cardiac disorders			Tachycardia		Ventricular arrhythmias, Torsades de pointes (reported predominantly in patients with risk factors for QT prolongation), ECG QT prolonged
Vascular disorders			Hypotension		
Respiratory, thoracic and mediastinal disorders		Cough, Nasopharyngitis	Dyspnoea, Brochospasm		Allergic pneumonitis, Severe dyspnoea
Gastrointestinal disorders		Abdominal pain, Diarrhoea, Nausea, Vomiting	Enterocolitis, sometimes haemorrhagic	*Pseudomembranous colitis*	
Hepatobiliary disorders			Hepatic enzymes increased (ALAT, ASAT, LDH, gamma-GT and/or alkaline phosphatase), Blood bilirubin increased	Jaundice cholestatic	Hepatitis, which may be severe
Skin and subcutaneous tissue disorders		Pruritus, Rash	Urticaria, Hot flushes, Hyperhidrosis, Pustular rash	Erythema multiforme, Toxic epidermal necrolysis, Photosensitivity reaction, Drug eruption Vascular purpura, Vasculitis, which can lead in exceptional cases to skin necrosis.	Stevens-Johnson syndrome; Acute generalized exanthemous pustulosis; drug rash
Musculoskeletal and Connective tissue disorders			Tendonitis	Arthralgia, Myalgia, Tendon rupture (e.g. Achilles tendon) which may occur within 48 hours of treatment start and may be bilateral.	Rhabdomyolysis and/or Myopathy, Muscular weakness, Muscle tear, Muscle rupture, Exacerbation of myasthenia gravis
Renal and Urinary disorders			Serum creatinine increased	Acute renal failure	Acute interstitial nephritis
Congenital and familial/genetic disorders					Attacks of porphyria in patients with porphyria

Symptoms and Treatment for Overdosage, and Antidote(s):
Overdosage of ofloxacin would be expected to produce manifestations that are extensions of the adverse reactions reported with the drug, and may include nausea, vomiting, seizures, vertigo, dysgeusia and psychosis.
If acute overdosage of ofloxacin occurs, the stomach should be emptied by inducing emesis or gastric lavage. Supportive and symptomatic treatment should be initiated, and patient should be observed carefully. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation. Adequate hydration should be maintained. Because ofloxacin is not efficiently removed by haemodialysis or peritoneal dialysis, these procedures should not be relied onto enhance elimination of the drug from the body.

Shelf-Life:
3 years from the date of manufacture.

Storage Condition(s):
Keep in a tight container. Store at temperature below 30°C. Protect from light and moisture.

Product Description & Packing(s):
Ofcin F.C. Tablet 200mg
A slight orange color film coated round tablet.
Plastic bottle of 500's and 1000's
Blister packing of 10's x 10 and 10's x 50

Ofcin F.C. Tablet 400mg
A slight orange color elliptical film coated tablet, one side impressed with a score.
Plastic bottle of 500's and 1000's
Blister packing of 10's x 10 and 10's x 50
(Not all presentations may be available locally)

Y. S. P.®

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