

OFLICIN TABLET

COMPOSITION:

OFLICIN-100:

Each tablet contains 100mg Ofloxacin

White to pale yellowish round shape film coated tablet

OFLICIN-200:

Each tablet contains 200mg Ofloxacin

White to pale yellowish, round shape film coated tablet, with a score line on one side.

ACTION:

Ofloxacin is a broad-spectrum bactericidal agent. It acts by inhibiting DNA synthesis in susceptible microorganisms. Ofloxacin has a broad spectrum antibacterial activity against various gram-negative and gram-positive organisms. It is effective against *Staphylococcus sp.*, *Hemolytic streptococcus*, enterococci, *E. coli*, *Klebsiella pneumoniae*, *Serratia* and *Proteus spp.*, *P. aeruginosa*, *H. influenza* and *N. gonorrhoeae*. Ofloxacin is also effective against nalidixic acid-resistant Enterobacteriaceae, Penicillin-resistant *N. gonorrhoeae*, gentamicin-resistant *P. aeruginosa* and anaerobic *Peptostreptococcus spp.* Maximum serum concentrations are achieved 2 to 3 hours after oral administration of ofloxacin as a single dose. The drug is well distributed and reaches high concentrations in various tissue and body fluids, including saliva, sputum, prostatic fluid, endometrium, skin, bile, gall-bladder, tears and gingiva. More than 90% of the drug is excreted unchanged in the urine, and urinary concentration increases dose-dependently.

Biological half-life of ofloxacin after a single oral dose of 100mg, 200mg and 300mg was about 3.6, 4.5 and 5.5 hours, respectively.

INDICATION:

Ofloxacin is indicated for the treatment of the following infections caused by susceptible organisms: Lower respiratory tract infections, urogenital tract infections, Skin & soft tissue infections including secondary infections in trauma, burns and operative wounds.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

DOSAGE AND ADMINISTRATION:

Dosage should be adjusted according to the severity of infection. The usual adult oral dose is 300-600mg daily divided into 2 to 3 doses, increased to 400-800mg daily if necessary. For lower respiratory tract infections: 300mg-600mg daily, increased to 800mg daily if necessary, for a duration of 10 days. For urogenital infections: 300mg-800mg daily for 7 to 10 days in urinary tract infections; 600mg daily for 7 days in nongonococcal and gonococcal urethritis and cervicitis. A single 400mg dose may be given for acute uncomplicated gonorrhoea.

In patients with impaired renal function, dosage adjustment should be as follows:

Creatinine clearance (ml/min) (ml/sec)	Dose %	Dosing interval (hr)
>50/0.83	100	12
10-50/0.17-0.83	100	24
<10/0.17	50	24

In patients undergoing haemodialysis or peritoneal dialysis, 100mg should be given every 24 hours. No dosage adjustment is required in impaired liver function since there is only limited metabolism of ofloxacin.

CONTRAINDICATIONS:

Ofloxacin is contraindicated in patients who are hypersensitive to the active ingredient or any other ingredients in the tablet, and in those who have previous allergic reactions to quinolones. It is contraindicated in those with a history of epilepsy as treatment with ofloxacin may trigger convulsion. Ofloxacin is also contraindicated in pregnant women and in children or adolescents in the growing phase as fluoroquinolones have been shown to cause arthropathy in immature animals.

WARNINGS AND PRECAUTIONS:

Ofloxacin should be administered with caution in patients with severe renal function impairment as persistent high serum levels have been reported. Tendonitis of the Achilles tendon may occur, which may lead to tendon rupture. If pain occurs in the Achilles tendon, the patient should be told to stop treatment and rest completely. As with other antibacterial agents, prolonged use of ofloxacin may cause overgrowth of nonsusceptible organisms. If superinfection occurs, discontinue the drug immediately.

Exacerbation of myasthenia gravis

Fluoroquinolones have neuromuscular blocking activity and may exacerbate muscle weakness in person with myasthenia gravis. Post marketing serious adverse events, including deaths and requirement for ventilator support have been associated with fluoroquinolones use in persons with myasthenia gravis. Avoid fluoroquinolones in patients with known history of myasthenia gravis.

Musculo-skeletal system

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 fluoroquinolone medication (Ofloxacin) and to contact their health care professional promptly about changing their antimicrobial therapy. Patients should also avoid exercise and using the affected area at the first sign of tendon pain, swelling or inflammation.

Psychiatric reactions

Psychiatric reactions may occur even after the first administration of fluoroquinolones, including Oflicin tablet. In rare cases, depression or psychotic reactions can progress to suicidal ideations/thoughts and self-injurious behaviour, such as attempted or completed suicide (see section side effects). In the event that the patient develops these reactions, Oflicin tablet should be discontinued and appropriate measures instituted. Caution is recommended if Oflicin tablet is to be used in psychotic patients or in patients with a history of psychiatric disease

The use of ofloxacin should be avoided in patients who have experienced serious adverse reactions in the past when using fluoroquinolones containing products (see section side effects). Treatment of these patients with ofloxacin should only be initiated in the absence of alternative treatment options and after careful benefit/risk assessment.

Aortic aneurysm and 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.

Prolonged, disabling and potentially irreversible serious adverse drug reactions

Very rare cases of prolonged (continuing months or years), disabling and potentially irreversible serious adverse drug reactions affecting different, sometimes multiple body systems (musculoskeletal, nervous, psychiatric and senses) have been reported in patients receiving fluoroquinolones irrespective of their age and pre-existing risk factors. Oflicin should be discontinued immediately at the first signs or symptoms of any serious adverse reaction and patients should be advised to contact their prescriber for advice.

Tendinitis and tendon rupture

Tendinitis and tendon rupture (especially but not limited to Achilles tendon), sometimes bilateral, may occur as early as within 48 hours of starting treatment with fluoroquinolones and have been reported to occur even up to several months after discontinuation of treatment. The risk of tendinitis and tendon rupture is increased in older patients (above 60 years of age), with renal impairment, patients with solid organ transplants, and those treated concurrently with corticosteroids*. Therefore, concomitant use of corticosteroids should be avoided.

At the first sign of tendinitis (e.g. painful swelling, inflammation) the treatment with Oflicin should be discontinued and alternative treatment should be considered. The affected limb(s) should be appropriately treated (e.g. immobilisation). Corticosteroids should not be used if signs of tendinopathy occur.

Peripheral neuropathy

Cases of sensory or sensorimotor polyneuropathy resulting in paraesthesia, hypaesthesia, dysesthesia, or weakness have been reported in patients receiving quinolones and fluoroquinolones. Patients under treatment with Oflicin should be advised to inform their doctor and pharmacist prior to continuing treatment if symptoms of neuropathy such as pain, burning, tingling, numbness, or weakness develop in order to prevent the development of potentially irreversible condition. (see section side effects).

EFFECTS ON ABILITY TO DRIVE AND USE MACHINE:

Ofloxacin may cause dizziness and light-headedness. If affected, the patient should not drive, operate machinery or engage in any activity that requires mental alertness and coordination.

PREGNANCY AND LACTATION:

Safety of ofloxacin in pregnant women has not been established and should be avoided in these patients.

Ofloxacin is excreted in milk. Therefore, it should not be administered to nursing mothers. However, if treatment is necessary for the benefit of the mother, then breastfeeding should be stopped.

Use in children:

Safety of ofloxacin in children has not been established.

Use in the elderly:

Ofloxacin should be used with caution in elderly patients since they may tend to have compromised renal function.

DRUG INTERACTIONS:

Concurrent administration of ofloxacin and theophylline may prolong half-life of theophylline, elevate serum theophylline levels and may increase the risk of theophylline-related adverse reactions. Administration of ofloxacin with antacids, sucralfate or other drugs containing calcium, magnesium, aluminium, iron or zinc (divalent or trivalent cations) substantially reduces the absorption of ofloxacin. These drugs not to be taken within two hours before or two hours after oral administration of ofloxacin. When ofloxacin is administered concurrently with warfarin or its derivatives, anticoagulant effect may be enhanced, hence prothrombin time should be monitored and the dose of warfarin adjusted where appropriate. Cimetidine may interfere with the elimination of some quinolones, resulting in significant increases in plasma half-life and AUC (area under the curve) of some quinolones. The potential for interaction between ofloxacin and cimetidine has not been studied. The concurrent administration of a non-steroidal anti-inflammatory agent with a quinolone, including ofloxacin, may increase the risk of central nervous system (CNS) stimulation and convulsive seizures. While the effect of probenecid on ofloxacin elimination has not been studied, concomitant use of probenecid with certain other quinolones has been reported to affect renal tubular secretion. When quinolones are used concurrently with antidiabetic agents (eg. insulin, glyburide / glibenclamide, etc), careful monitoring of blood sugar is recommended. This is because disturbances of blood glucose, including hyperglycaemia and hypoglycaemia, have been reported in patients treated concurrently with quinolones and an antidiabetic.

SIDE-EFFECTS:

Adverse effects which may occur rarely: shock, anaphylaxis, toxic epidermal necrolysis, Stevens-Johnson syndrome, convulsion, mucocutaneous ocular syndrome, acute renal failure, jaundice, interstitial pneumonia, agranulocytosis, pseudomembranous colitis, rhabdomyolysis, hypoglycaemia (especially in patients with diabetes mellitus or renal diseases). Tendonitis, neurological disturbances (eg headache, dizziness, sleep disturbances, numbness, hallucinations, confusion), elevated liver enzyme levels, malaise, arthralgia, taste abnormalities and gastrointestinal disturbances may also occur. Cardiovascular adverse events such as changes in blood pressure (hypertension, postural hypotension), palpitations, oedema have been reported very rarely during clinical trials with ofloxacin. If hypersensitivity reactions or haematologic changes (eg. anaemia, thrombocytopenia, leukopenia) occurs, discontinue treatment immediately.

Exacerbation of myasthenia gravis

Post Marketing Experience

Psychiatric disorders

Rare: Psychotic disorder (for e.g.hallucination)

Very Rare: Psychotic behaviour

Frequency not known (cannot be estimated from the available data):

Psychotic disorders and depression with self-endangering behavior including suicidal ideation or suicide attempt

Musculoskeletal and connective tissue disorders*

Nervous system disorders*

General disorders and administrative site conditions*

Psychiatric disorders*

Eye disorders*

Ear and labyrinth disorders*

*Very rare cases of prolonged (up to months or years), disabling and potentially irreversible serious drug reactions affecting several, sometimes multiple, system organ classes and senses (including reactions such as tendinitis, tendon rupture, arthralgia, pain in extremities, gait disturbance, neuropathies associated with paraesthesia, depression, fatigue, memory impairment, sleep disorders, and impairment of hearing, vision, taste and smell) have been reported in association with the use of fluoroquinolones in some cases irrespective of pre-existing risk factors (see section Warnings and Precautions).

OVERDOSAGE:

If overdosage occurs, treatment should be symptomatic. Induction of emesis or a gastric lavage may be performed to remove any unabsorbed drug. The patient should be monitored for his vital signs.

STORAGE:

Store in a cool dry place below 30°C.

Protect from light.

Keep out of reach of children.

PRESENTATION:

Blister strips of 10 tablets; 100 tablets per box.

MANUFACTURED BY:

Noripharma Sdn Bhd, Lot 5030, Jalan Teratai,

5 1/2 Mile off Jalan Meru,

41050 Klang, Selangor D.E, Malaysia.

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