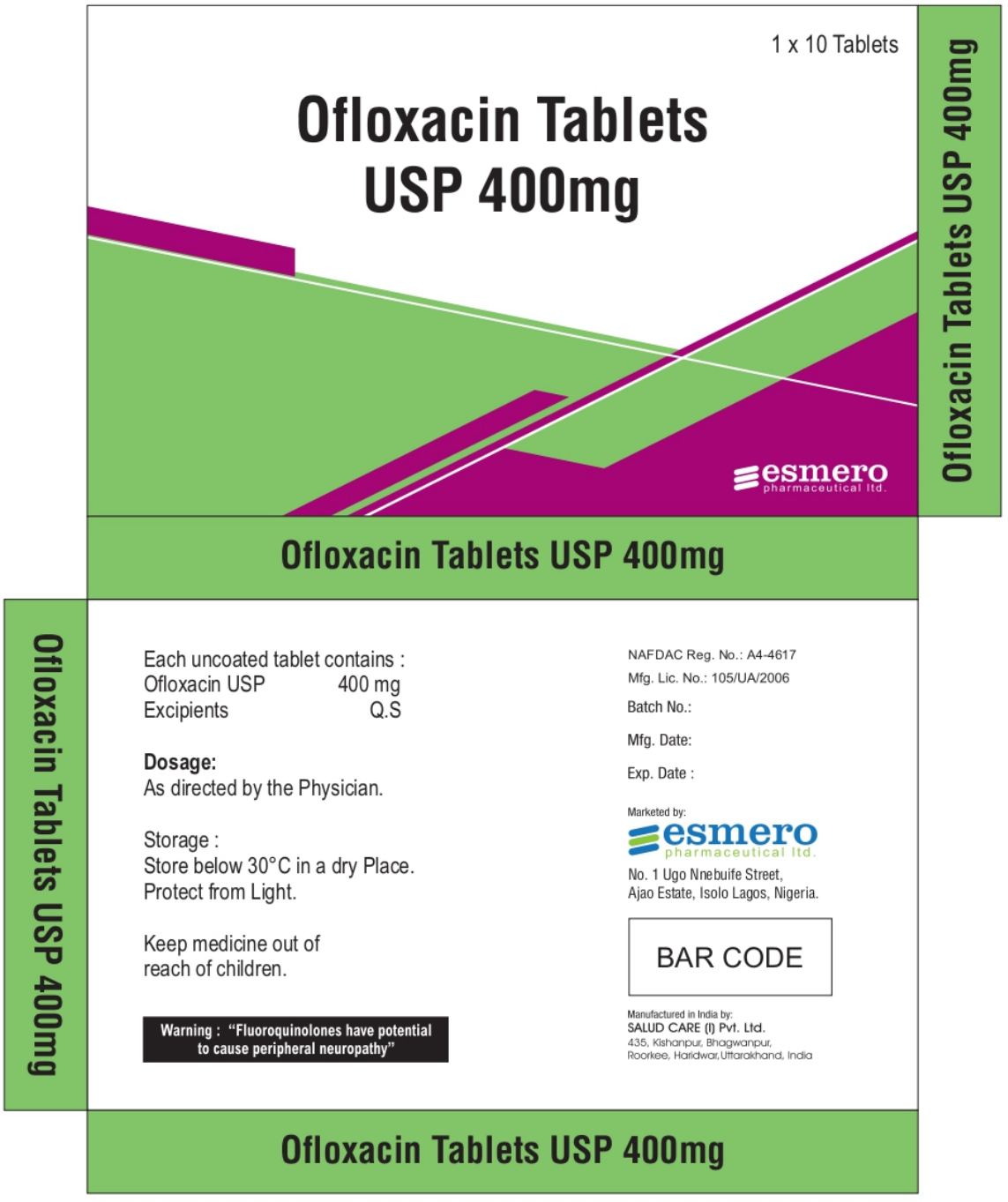
SIZE : L-130, W-13, H-80 MM



5. PRODUCT INFORMATION: SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

SUMMARY OF PRODUCT CHARECTERISTICS

Ofloxacin Tablets USP 400mg

1. Name of the medicinal product

Generic Name: Ofloxacin Tablets USP 400mg

2. Qualitative and quantitative composition

Each film coated tablet contains 400 mg of Ofloxacin.

For a full list of excipients, see section 6.1

3. Pharmaceutical form

Film coated Tablets

Description: A white colored, elongated shape, biconvex, film coated tablet having a break line on one side of each tablet.

4. Clinical Particulars

4.1 Therapeutic indications

Ofloxacin is a synthetic 4-fluoroquinolone antibacterial agent with bactericidal activity against a wide range of Gram-negative and Gram-positive organisms. It is indicated for the treatment of the following infections when caused by sensitive organisms: Upper and lower urinary tract infections; lower respiratory tract infections; uncomplicated urethral and cervical gonorrhoea; non-gonococcal urethritis and cervicitis, skin and soft tissue infections.

4.2 Posology and method of administration

For oral use.

General dosage recommendations: The dose of ofloxacin is determined by the type and severity of the infection. The dosage range for adults is 200mg to 800mg daily. Up to 400mg may be given as a single dose, preferably in the morning, larger doses should be given as two divided doses. Generally, individual doses are to be given at approximately equal intervals. Ofloxacin tablets should be swallowed with liquid; they should not be taken within two hours of magnesium/aluminium containing antacids, sucralfate, zinc or iron preparations since reduction of absorption of ofloxacin can occur.

Lower urinary tract infection: 200-400 mg daily.

Upper urinary tract infection: 200-400 mg daily increasing, if necessary, to 400 mg twice a day.

Lower respiratory tract infection: 400 mg daily increasing, if necessary, to 400 mg twice daily.

Uncomplicated urethral and cervical gonorrhoea: A single dose of 400 mg.

Non-gonococcal urethritis and cervicitis: 400 mg daily in single or divided doses.

Skin and soft tissue infections: 400 mg twice daily.

Impaired renal function: Following a normal initial dose, dosage should be reduced in patients with impairment of renal function. When creatinine clearance is 20-50 ml/minute (serum creatinine 1.5-5.0 mg/dl) the dosage should be reduced by half (100-200 mg daily). If creatinine clearance is less than 20 ml/minute (serum creatinine greater than 5 mg/dl) 100 mg should be given every 24 hours. In patients undergoing haemodialysis or peritoneal dialysis, 100 mg should be given every 24 hours.

Impaired liver function: The excretion of ofloxacin may be reduced in patients with severe hepatic dysfunction.

Elderly: No adjustment of dosage is required in the elderly, other than that imposed by consideration of renal or hepatic function (See section 4.4 QT interval prolongation).

Children: Ofloxacin is not indicated for use in children or growing adolescents.

Duration of treatment: Duration of treatment is dependent on the severity of the infection and the response to treatment. The usual treatment period is 5-10 days except in uncomplicated gonorrhoea, where a single dose is recommended.

Treatment should not exceed 2 months duration.

4.3 Contraindications

Ofloxacin should not be used in patients with known hypersensitivity to 4-quinolone antibacterials or any of the tablet excipients.

Ofloxacin should not be used in patients with a past history of tendinitis.

Ofloxacin, like other 4-quinolones, is contra-indicated in patients with a history of epilepsy or with a lowered seizure threshold.

Ofloxacin is contra-indicated in children or growing adolescents, and in pregnant or breast-feeding women, since animal experiments do not entirely exclude the risk of damage to the cartilage of joints in the growing subject.

Patients with latent or actual defects in glucose-6-phosphate dehydrogenese activity may be prone to haemolytic reactions when treated with quinolone antibacterial agents.

4.4 Special warnings and precautions for use

Ofloxacin is not the drug of first choice for pneumonia caused by Pneumococci or Mycoplama, or angina tonsillaris caused by β-haemolytic Streptococci.

Hypersensitivity and allergic reactions have been reported for fluoroquinolones after first administration. Anaphylactic and anaphylactoid reactions can progress to life-threatening shock, even after the first administration. In these cases ofloxacin should be discontinued and suitable treatment (e.g treatment for shock) should be initiated.

Clostridium difficile-associated disease

Diarrhoea, particularly if severe, persistent and/or bloody, during or after treatment with ofloxacin, may be symptomatic of pseudo-membranous colitis. If pseudo-membranous colitis is suspected, ofloxacin must be stopped immediately. Appropriate specific antibiotic therapy must be started without delay (e.g. oral vancomycin, oral teicoplanin or metronidazole). Products inhibiting the peristalsis are contraindicated in this clinical situation

Patients predisposed to seizures

In case of convulsive seizures, treatment with ofloxacin should be discontinued (see section 4.5 lowering of the cerebral seizure threshold).

Cardiac Disorders

Very rare cases of QT interval prolongation have been reported in patients taking fluoroquinolones. 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)

- cardiac disease (e.g. heart failure, myocardial infarction, bradycardia)

Elderly patients and women may be more sensitive to QTc-prolonging medications. Therefore, caution should be taken when using fluoroquinolones, including Ofloxacin, in these populations.
(See section 4.2 Elderly, section 4.5, section 4.8 section 4.9).
Patients being treated with ofloxacin should not expose themselves unnecessarily to strong sunlight and should avoid UV rays (sun lamps, solaria).

Patients with history of psychotic disorder

Psychotic reactions have been reported in patients receiving fluoroquinolones. In some cases these have progressed to suicidal thoughts or self-endangering behaviour including suicide attempt, sometimes after a single dose. In the event that a patient develops these reactions, ofloxacin should be discontinued and appropriate measures instituted. Ofloxacin should be used with caution in patients with a history of psychotic disorder or in patients with psychiatric disease.

Patients with impaired liver function

Ofloxacin should be used with caution in patients with impaired liver function, as liver damage may occur. Cases of fulminant hepatitis potentially leading to liver failure (including fatal cases) have been reported with fluoroquinolones. Patients should be advised to stop treatment and contact their doctor if signs and symptoms of hepatic disease develop such as anorexia, jaundice, dark urine, pruritis or tender abdomen. (See section 4.8: Undesirable effects)

Patients treated with vitamin K antagonists

Due to possible increase in coagulation tests (PT/INR) and/or bleeding in patients treated with fluoroquinolones, including ofloxacin, in combination with a vitamin K antagonist (e.g.warfarin), coagulation tests should be monitored when these drugs are given concomitantly (see section 4.5)

Myasthenia gravis

Ofloxacin should be used with caution in patients with a history of myasthenia gravis. Administration of antibiotics, especially of prolonged, may lead to proliferation of resistant micro-organisms. The patient's condition must therefore be checked at regular intervals. If a secondary infection occurs, appropriate measures must be taken.

Peripheral neuropathy

Sensory or sensorimotor peripheral neuropathy has been reported in patients receiving fluoroquinolones, including ofloxacin. Ofloxacin should be discontinued if the patient experiences symptoms of neuropathy in order to prevent the development of an irreversible condition.

Hypoglycaemia

As with all quinolones, hypoglycaemia has been reported, usually in diabetic patients receiving concomitant treatment with an oral hypoglycaemic agent (e.g. glibenclamide) or with insulin. In these diabetic patients, careful monitoring of blood glucose is recommended.

Patients with glucose-6-phosphate-dehydrogenase deficiency

Patients with latent or diagnosed glucose-6-phosphate-dehydrogenase deficiency may be predisposed to haemolytic reactions if they are treated with quinolones. Ofloxacin should therefore be administered with caution in such patients.

Patients with rare hereditary disorders

Patients with rare hereditary disorders of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

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) (See section 4.4).

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.

Prolongation of bleeding time has been reported during concomitant administration of OFLOXACIN TABLETS USP 400mg and anticoagulants.

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.

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

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, frusemide 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.

Vitamin K antagonists

Coagulation tests should be monitored in patients treated with vitamin K antagonists because of a possible increase in the effect of coumarin derivatives.

4.6 Pregnancy and lactation

Based on a limited amount of human data, the use of fluoroquinolones in the first trimester of pregnancy has not been associated with an increased risk of major malformations or other adverse effects on pregnancy outcome. Animal studies have shown damage to the joint

cartilage in immature animals but no teratogenic effects. Therefore ofloxacin should not be used during pregnancy. (See section 4.3: Contraindications)

Ofloxacin is excreted into human breast milk in small amounts. Because of the potential for arthropathy and other serious toxicity in the nursing infant, breast feeding should be discontinued during treatment with ofloxacin. (See section 4.3: Contraindications)

4.7 Effects on ability to drive and use machines

Since there have been occasional reports of somnolence, impairment of skills, dizziness and visual disturbances, patients should know how they react to OFLOXACIN TABLETS USP 400mg before they drive or operate machinery. These effects may be enhanced by alcohol.

4.8 Undesirable effects

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 (cannot be estimated from available data)*
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 (see Section 4.4)
Psychiatric disorders		Agitation, Sleep disorder, Insomnia	Psychotic disorder (for e.g. hallucination),		Psychotic disorder and depression with self-endangering

			Anxiety, Confusional state, Nightmares, Depression		behaviour including suicidal ideation or suicide attempt (see Section 4.4)
Nervous system disorders		Dizziness, Headache	Somnolence, Paraesthesia, Dysgeusia, Parosmia	Peripheral sensory neuropathy* Peripheral sensory motor neuropathy* Convulsion*, Extra-pyramidal symptoms or other disorders of muscular coordination	
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 (see section 4.4 and 4.9)
Vascular disorders	*applies only to the solution for infusion*: Phlebitis		Hypotension		*applies only to the solution for infusion*: During infusion of ofloxacin, tachycardia and hypotension may occur. Such a decrease in blood pressure may, in very rare cases, be severe.
Respiratory, thoracic and		Cough, Naso-	Dyspnoea, Bronchospasm		Allergic pneumonitis,

mediastinal disorders		pharyngitis			Severe dyspnoea
Gastrointestinal disorders		Abdominal pain, Diarrhoea, Nausea, Vomiting	Enterocolitis, sometimes haemorrhagic	Pseudo-membranous colitis*	
Hepatobilary 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, Photo-sensitivity 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
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
General disorders and	*applies only to the*				

administration site conditions	*solution for infusion*: Infusion site reaction (pain, reddening)				

* postmarketing experience

4.9 Overdose

The most important signs to be expected following acute overdosage are CNS symptoms such as confusion, dizziness, impairment of consciousness and convulsive seizures as well as gastrointestinal reactions such as nausea and mucosal erosions.

In the case of overdose steps to remove any unabsorbed ofloxacin eg gastric lavage, administration of adsorbants and sodium sulphate, if possible during the first 30 minutes, are recommended; antacids are recommended for protection of the gastric mucosa.

Elimination of ofloxacin may be increased by forced diuresis.
In the event of overdose, symptomatic treatment should be implemented. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Quinolone antibacterials, Fluoroquinolones. ATC code J01M A01

Ofloxacin is a quinolone-carboxylic acid derivative with a wide range of antibacterial activity against both gram negative and gram positive organisms. It is active after oral administration. It inhibits bacterial DNA replication by blocking DNA topo-isomerases, in particular DNA gyrase.

Therapeutic doses of ofloxacin are devoid of pharmacological effects on the voluntary or autonomic nervous systems.

Microbiological results indicate that the following pathogens may be regarded as sensitive: *Staphylococcus aureus*(including methicillin resistant staphylococci), *Staphylococcus epidermidis*, Neisseria species, *Escherichia coli*, Citrobacter, Klebsiella, Enterobacter, Hafnia, Proteus (indole-negative and indole-positive strains), *Haemophilus influenzae*, Chlamydiae, Legionella, Gardnerella.

Variable sensitivity is shown by Streptococci, *Serratia marcescens*, *Pseudomonas aeruginosa* and Mycoplasmas.

Anaerobic bacteria (e.g. Fusobacterium species, Bacteroides species, Eubacterium species, Peptococci, Peptostreptococci) are normally resistant.

5.2 Pharmacokinetic properties

Ofloxacin is almost completely absorbed after oral administration. Maximal blood levels occur 1-3 hours after dosing and the elimination half-life is 4-6 hours. Ofloxacin is primarily excreted unchanged in the urine.

In renal insufficiency the dose should be reduced.

No clinically relevant interactions were seen with food and no interaction was found between ofloxacin and theophylline.

5.3 Preclinical safety data

Not Applicable

6. Pharmaceutical particulars

6.1 List of excipients

Sr. No	Ingredient	Specification	Function
1.	Maize starch	BP-2014	Diluent
2.	Microcrystalline Cellulose	BP-2014	Diluent
3.	Sodium Methyl Hydroxybenzoate	BP-2014	Preservative
4.	Sodium Propyl Hydroxybenzoate	BP-2014	Preservative
5.	Citric Acid Monohydrate	BP-2014	Buffering Agent
6.	Maize Starch	BP-2014	Binder
7.	Purified Water	BP-2014	Solvent for binder
8.	Talc	BP-2014	Glidant
9.	Magnesium Stearate	BP-2014	Anti-adherent
10	Sodium Starch Glycolate	BP-2014	Disintegrant
Coating material			
11.	Protectab HP – 1 (organic)	IH	Film coating

			material
12.	Isopropyl Alcohol	BP-2014	Solvent
13.	Dichloromethane	BP-2014	Solvent
14.	Titanium Dioxide	BP-2014	Colorant

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Do not store above 30°C. Protect from light.

6.5 Nature and contents of container

10 x10 Alu.Alu Pack

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketed by

Esmero Pharmaceutical ltd

Nigeria

8. Manufactured in India by

Salud Care (I) Pvt. Ltd.

Roorkee, Uttarakhand, India.

9. Date of first authorization/renewal of the authorization

Not applicable

10. Date of revision of the text

Not applicable