SUMMARY OF PRODUCT CHARACTERISTICS

APPROVED
By Geeta at 9:57 am, Feb 04, 2019

1 NAME OF THE MEDICINAL PRODUCT

Ofloxacin 400mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 400 mg of ofloxacin.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film coated tablets (tablet)
The tablets are white capsule shaped and scored on both sides with 'BL' and '400' debossed on one face of the tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Ofloxacin is indicated in adults for the treatment of the following bacterial infections (see sections 4.4 and 5.1):
- Pyelonephritis and complicated urinary tract infections
- Prostatitis, epididymo-orchitis
- Pelvic inflammatory disease, in combination treatment
- Upper and lower urinary tract infections
- Uncomplicated urethral and cervical gonorrhea
- Non gonococcal urethritis and cervicitis

For the below-mentioned infections ofloxacin should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the initial treatment of these infections (see section 4.4):
- Uncomplicated cystitis
- Urethritis
- Complicated skin and soft-tissue infections
- Acute exacerbation of chronic bronchitis

- Community acquired pneumonia
Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

General dosage recommendations: The dose of ofloxacin is determined by the type and severity of the infection. The dosage range for adults is 200 mg to 800 mg daily. A daily dose of up to 400 mg ofloxacin may be given as a single dose. In this case, it is preferable to administer ofloxacin in the morning. Larger doses should be given as two divided doses. Generally, individual doses are to be given at approximately equal intervals. Ofloxacin Film-coated tablets are to be swallowed with sufficient amount of liquids. They may be taken on an empty stomach or with meals. Concomitant administration with antacids should be avoided (see section 4.5: Interactions).
Lower urinary tract infection: 200-400mg daily.

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

Acute exacerbation of chronic bronchitis, community acquired pneumonia: 400 mg daily increasing, if necessary, to 400mg twice daily.

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

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

Complicated skin and soft tissue infections: 400mg twice daily.

Acute exacerbation of chronic bronchitis, community acquired pneumonia: 400 mg daily increasing, if necessary, to 400 mg twice daily.
Complicated skin and soft tissue infections: 400 mg twice daily.

Indication	**Daily dose regimen** *(according to severity)*	**Duration of treatment** *(according to severity)*
Complicated UTI	200 mg twice daily (can be increased to 400 mg twice daily)	7-21 days
Pyelonephritis	200 mg twice daily (can be increased to 400 mg twice daily)	7-10 days (can be extended to 14 days)
Acute prostatitis Chronic prostatitis	200 mg twice daily (can be increased to 400 mg twice daily)	2-4 weeks* 4-8 weeks*
Epididymo-orchitis	200 mg twice daily (can be increased to 400 mg twice	14 days

	daily)	
Pelvic inflammatory disease	400 mg twice daily	14 days
Uncomplicated cystitis	200 mg twice daily or 400 mg once daily	3 days 1 day
Complicated cystitis	200 mg twice daily	7-14 days
Non-gonococcal urethritis	300 mg twice daily	7 days
Neisseria gonorrhoeae urethritis See section 4.4	400 mg single dose	1 day

*for prostatitis longer duration of treatment may be considered after careful re-examination of the patient.
Ofloxacin may also be used to complete a course of therapy in patients who have shown improvement during initial treatment with intravenous ofloxacin.

Posology in patients with renal insufficiency:
In patients with impaired renal function, the following oral or I.V. dosages are recommended:

CREATININE CLEARANCE	UNIT DOSE mg*	NUMBER / 24 h	INTERVALS h
50 – 20 ml/min	100-200	1	24
< 20 ml/min** or haemodialysis or peritoneal dialysis	100 or 200	1 1	24 48

* According to indication or dose interval.

** The serum concentration of ofloxacin should be monitored in patients with severe renal impairment and dialysis patients.

When creatinine clearance cannot be measured, it can be estimated with reference to the serum creatinine level using the following Cockcroft's formula for adults:

$$\text{Men:} \quad \text{ClCr (ml/min)} = \frac{\text{weight(kg)} \times (140 - \text{age in years})}{72 \times \text{serum creatinine (mg/dl)}}$$

or

$$\text{ClCr (ml/min)} = \frac{\text{weight(kg)} \times (140 - \text{age in years})}{0.814 \times \text{serum creatinine } (\mu\text{mol/l})}$$

Women: ClCr (ml/min) = 0.85 x (above value)

Posology in hepatic insufficiency (e.g. cirrhosis with ascites)

It is recommended that a maximum daily dose of 400 mg of ofloxacin be not exceeded, because of possible reduction of excretion.

Elderly: Age in itself does not impose to adapt the dosage of ofloxacin. However, special attention to renal function should be paid in elderly patients, and the dosage should be adapted accordingly. (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 other quinolones antibacterials, or any of the other excipients listed in section 6.1.

Ofloxacin should not be used in patients with a past history of tendinitis related to fluoroquinolone administration.

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

Ofloxacin is contraindicated 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 dehydrogenase activity may be prone to haemolytic reactions when treated with quinolone antibacterial agents.

4.4 Special warnings and precautions for use

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.

Methicillin-resistant S. aureus are very likely to possess co-resistance to fluoroquinolones, including ofloxacin. Therefore ofloxacin is not recommended for the treatment of known or suspected MRSA infections unless laboratory results have confirmed susceptibility of the organism to ofloxacin (and commonly recommended antibacterial agents for the treatment of MRSA-infections are considered inappropriate).

Escherichia coli infection

Resistance to fluoroquinolones of *E. coli* – the most common pathogen involved in urinary tract infections – varies across the European Union. Prescribers are advised to take into account the local prevalence of resistance in *E. coli* to fluoroquinolones. Ofloxacin is not the drug of first choice for pneumonia caused by Pneumococci or Mycoplasma or infection caused by β-haemolytic Streptococci.

Neisseria gonorhoeae infections

Due to increase in resistance to N. gonorrhoeae, ofloxacin should not be used as empirical treatment option in suspected gonococcal infection (urethral gonococcal infection, pelvic inflammatory disease and epididymo-orchitis), unless the pathogen has been identified and confirmed as susceptible to ofloxacin. If clinical improvement is not achieved after 3 days of treatment, the therapy should be reconsidered.

Pelvic inflammatory disease

For pelvic inflammatory disease, ofloxacin should only be considered in combination with anaerobe coverage.

Hypersensitivity and allergic reactions

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.

Severe bullous reactions
Cases of severe bullous skin reactions such as Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported with ofloxacin (see section 4.8). Patients should be advised to contact their doctor immediately prior to continuing treatment if skin and/or mucosal reactions occur.

Clostridium difficile-associated disease
Diarrhoea, particularly if severe, persistent and/or bloody, during or after treatment with ofloxacin (including several weeks after treatment), may be symptomatic of pseudo-membranous colitis (CDAD). CDAD may range in severity from mild to life threatening, the most severe form which is pseudomembranous colitis (see section 4.8). It is therefore important to consider this diagnosis in patients who develop serious diarrhoea during or after treatment with ofloxacin .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
Quinolones may lower the seizure threshold and may trigger seizures. Ofloxacin is contraindicated in patients with a history of epilepsy (see section 4.3) and, as with other quinolones, ofloxacin should be used with extreme caution in patients predisposed to seizures.

Such patients may be patients with pre-existing central nervous system lesions, concomitant treatment with fenbufen and similar non-steroidal anti-inflammatory drugs or with drugs which lower the cerebral seizure threshold, such as theophylline (see section 4.5: Interactions).

In case of convulsive seizures, treatment with ofloxacin should be discontinued

Tendinitis
Tendinitis, rarely observed with quinolones, may occasionally lead to rupture involving Achilles tendon in particular. Tendinitis and tendon rupture, sometimes bilateral, may occur within 48 hours of starting treatment with ofloxacin and have been reported up to several months after discontinuation of. The risk of tendinitis and tendon rupture is increased in patients aged over 60 years and in patients using corticosteroids. Furthermore, as transplanted patients are at increased risk of tendinitis, caution is recommended when fluoroquinolones are used in this population. The daily dose should be adjusted

in elderly patients based on creatinine clearance (see section 4.2). Close monitoring of these patients is therefore necessary if they are prescribed ofloxacin. All patients should consult their physician if they experience symptoms of tendinitis. If tendinitis is suspected, treatment with ofloxacin must be halted immediately, and appropriate treatment (e.g. immobilisation) must be initiated for the affected tendon (see sections 4.3 and 4.8).

Patients with renal impairment
Since ofloxacin is mainly excreted by the kidneys, the dose of ofloxacin should be adjusted in patients with renal impairment (see section 4.2).

QT interval prolongation
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, section 4.5, section 4.8 and section 4.9).

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 (see section 4.8). 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

Fluoroquinolones, including ofloxacin, have neuromuscular blocking activity and may exacerbate muscle weakness in patients with myasthenia gravis. Postmarketing serious adverse reactions, including deaths and the requirement for respiratory support, have been associated with fluoroquinolone use in patients with myasthenia gravis. Ofloxacin is not recommended in patients with a known history of myasthenia gravis

Prevention of photosensitisation

Photosensitisation has been reported with ofloxacin (see section 4.8). It is recommended that patients should not expose themselves unnecessarily to strong sunlight or to artificial UV rays (e.g. sunray lamp, solarium), during treatment and for 48 hours following treatment discontinuation in order to prevent photosensitisation

Superinfection

As with other antibiotics, the use of ofloxacin, especially if prolonged, may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If secondary infection occurs during therapy, appropriate measures should be taken.

Peripheral neuropathy

Sensory or sensorimotor peripheral neuropathy has been reported in patients receiving fluoroquinolones, including ofloxacin, which can be rapid in its onset. Ofloxacin should be discontinued if the patient experiences symptoms of neuropathy in order to prevent the development of an irreversible condition (see section 4.8).

Dysglycaemia

As with all quinolones, disturbances in blood glucose, including both hyperglycaemia and hypoglycaemia have been reported, usually in diabetic patients receiving concomitant treatment with an oral hypoglycaemic agent (e.g. glibenclamide) or with insulin. Cases of hypoglycaemic coma have been reported. In these diabetic patients, careful monitoring of blood glucose is recommended (see section 4.8).

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. Therefore, if ofloxacin has to be used in these patients, potential occurrence of haemolysis should be monitored.

Vision disorders
If vision becomes impaired or any effects on the eyes are experienced, an eye specialist should be consulted immediately (see sections 4.7 and 4.8).

Interference with laboratory tests
In patients treated with ofloxacin, determination of opiates in urine may give false- positive results. It may be necessary to confirm positive opiate screens by more specific method.

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 antiarrhythmics, 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 and anticoagulants.

Theophylline, fenbufen or similar non-steroidal anti-inflammatory drugs
No pharmacokinetic interactions of ofloxacin were found with theophylline in a clinical study. However, a pronounced lowering of the cerebral seizure threshold may occur when quinolones are given concurrently with theophylline, nonsteroidal anti-inflammatory drugs, or other agents, which lower the seizure threshold.

In case of convulsive seizures, treatment with ofloxacin should be discontinued.

Glibenclamide

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

Probenecid, cimetidine, furosemide and methotrexate Probenecid decreased the total clearance of ofloxacin by 24%, and increased AUC by 16%. The proposed mechanism is a competition or inhibition for active transport at the renal tubular excretion. Caution should be exercised when ofloxacin is coadministered with drugs that affect the tubular renal secretion such as probenecid, cimetidine, furosemide and methotrexate.

Vitamin K antagonists Increased coagulation tests (PT/INR) and/or bleeding, which may be severe, have been reported in patients treated with ofloxacin in combination with a vitamin K antagonist (e.g. warfarin). Coagulation tests should be monitored in patients treated with vitamin K antagonists (see section 4.4) because of a possible increase in the effect of coumarin derivatives.

4.6. Fertility, pregnancy and lactation

Pregnancy

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)

Breast-feeding

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 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) Hyperglycaemia

					Hypoglycaemic coma
Psychiatric disorders		Agitation, Sleep disorder, Insomnia	Psychotic disorder (for e.g. hallucination), Anxiety, Confusional state, Nightmares, Depression		Psychotic disorder and depression with self-endangering behaviour including suicidal ideation or suicide attempt (see Section 4.4) Nervousness
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	Tremor Dyskinesia Ageusia Syncope
Eye disorders		Eye irritation	Visual disturbance		Uveitis
Ear and labyrinth disorders		Vertigo		Tinnitus, Hearing loss	Hearing impaired
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 mediastinal disorders		Cough, Nasopharyngitis	Dyspnoea, Bronchospasm		Allergic pneumonitis, Severe dyspnoea
Gastrointestinal disorders		Abdominal pain, Diarrhoea, Nausea, Vomiting	Enterocolitis, sometimes haemorrhagic	Pseudomembranous colitis* Jaundice cholestatic	Dyspepsia Flatulence Constipation Pancreatitis
Hepatobiliary disorders			Hepatic enzymes increased (ALAT, ASAT, LDH, gamma-GT and/or		Hepatitis, which may be severe, Severe liver injury, including cases with acute liver failure,

			alkaline phosphatase) Blood bilirubin increased		sometimes fatal, have been reported with ofloxacin, primarily in patients with underlying liver disorders (see section 4.4).
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 Stomatitis Exfoliative dermatitis
Musculoskeletal and Connective tissue disorders			Tendinitis	Arthralgia, Myalgia, Tendon rupture (e.g. Achilles tendon) which may occur within 48 hours of treatment start and may be	Rhabdomyolysis and/or Myopathy, Muscular weakness Muscle tear, muscle rupture Ligament rupture Arthritis

				bilateral.	
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 administration site conditions	*applies only to the solution for infusion:* Infusion site reaction (pain, reddening)				Asthenia Pyrexia Pain (including pain in back, chest, and extremities)

* post-marketing experience

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme at:www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

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

CNS effects including confusional state, convulsion, hallucination, and tremor have been observed in post marketing experience

In the case of overdose steps to remove any unabsorbed ofloxacin e.g. gastric lavage, administration of adsorbants and sodium sulfate, if possible during the first 30 minutes, are recommended; antacids are recommended for protection of the gastric mucosa. A fraction of ofloxacin may be removed from the body with haemodialysis. Peritoneal dialysis and CAPD are not effective in removing ofloxacin from the body. No specific antidote exists.

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.

Mechanism of action

Ofloxacin is a quinolone-carboxylic acid derivative with a wide range of antibacterial activity against both gram-positive and gram-negative organisms. It is active after oral administration.
The primary mode of action of the quinolones is the specific inhibition of bacterial DNA gyrase. This enzyme is required for DNA replication, transcription, repair and recombination. Its inhibition leads to expansion and destabilisation of the bacterial DNA and hence to cell death.
It appears that certain quinolones, including ofloxacin, have a second non RNA dependent action on bacterial cells, which enhances bactericidal effectiveness. The nature of this second action has not yet been clarified

PK/PD relationship

Fluoroquinolones have a concentration-dependent bactericidal activity, with a moderate post antibiotic effect. For this class of antimicrobials, the ratio between AUC and MIC or Cmax and MIC is predictive of clinical success.

Mechanisms of resistance

Resistance to ofloxacin is acquired through a stepwise process by target site mutations in both type II topoisomerases, DNA gyrase and topoisomerase IV. Other resistance mechanisms such as permeation barriers (common in

Pseudomonas aeruginosa) and efflux mechanisms may also affect susceptibility to ofloxacin

Susceptibility testing breakpoints
Breakpoints separate susceptible strains from strains with intermediate susceptibility and the latter from resistant strains.
Breakpoints set by EUCAST:

Microorganism	**MIC breakpoint (mg/L)**	
	Susceptible ≤	**Resistant >**
Enterobacteriaceae	0.5	1
Staphylococcus spp.	1	1[a]
Streptococcus pneumoniae[b]	0.125	4
Haemophilus influenzae	0.5	0.5
Moraxella catarrhalis	0.5	0.5
Neisseria gonorrheae	0.125	0.25
a. Breakpoints relate to high dose therapy b. Wild type *S. pneumonia* are not considered susceptible to ofloxacin and are therefore categorized as intermediate		

Susceptibility
The prevalence of resistance may vary geographically and over time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species, including microorganisms with intermediate susceptibility
Aerobic Gram-positive micro-organisms *Bacillus anthracis* *Bordetella pertussis* Corynebacteria *Streptococci*
Aerobic Gram-negative micro-organisms Campylobacter Enterobacter *Haemophilus influenzae* *Legionella pneumophila* *Moraxella catarrhalis* *Morganella morganii*

Proteus vulgaris Salmonella Shigella Yersinia
Other micro-organisms Chlamydia *Chlamydophila pneumonia* *Mycoplasma hominis* *Mycoplasma pneumoniae* *Ureaplasma urealyticum*
Species for which acquired resistance may be a problem
Aerobic Gram-positive micro-organisms *Staphylococci coagulase negative* *Staphylococcus aureus (methicillin-sensitive)* *Streptococcus pneumoniae*
Aerobic Gram-negative micro-organisms *Acinetobacter baumannii* *Citrobacter freundii* *Escherichia coli* *Klebsiella oxytoca* *Klebsiella pneumoniae* *Neisseria gonorrhoeae* *Proteus mirabilis* *Pseudomonas aeruginosa* Serratia
Inherently resistant organisms
Aerobic Gram-positive micro-organisms Enterococci *Listeria monocytogenes* Nocardia Staphylococci methi-R
Anaerobic micro-organisms Bacteroides spp. *Clostridium difficile*

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

5.2 Pharmacokinetic properties

Ofloxacin is almost completely absorbed after oral administration. The peak serum concentration, after a single dose of 200 mg, averages 2.5 to 3µg/ml

within one hour. The serum elimination half-life is 6-7 hours and is linear. The apparent volume of distribution is 120 litres. Following multiple dosing, the serum concentration is not significantly increased (multiplication factor approximately 1.5). Ofloxacin concentrations in the urine and at the site of urinary tract infections exceed those measured in serum by 5 to 100-fold. 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

Microcrystalline cellulose
Sodium starch glycolate
Hydroxypropyl cellulose
Magnesium stearate
Hypromellose
Macrogol 400
Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable

6.3. Shelf life

3 years.

6.4. Special precautions for storage

Do not store above 25°C.
Store in the original package.

6.5 Nature and contents of container

Ofloxacin 400mg Tablets are available in blister packs of 5, 10 and 50 tablets in Alu/PVC blisters.

6.6 Special precautions for disposal

Not special requirements

7. MARKETING AUTHORISATION HOLDER

Bristol Laboratories Ltd
Unit 3, Canalside,
Northbridge Road,
Berkhamsted,
Hertfordshire HP4 1EG
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 17907/0025

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22/03/2004

10 DATE OF REVISION OF THE TEXT

04/02/2019