The format of this leaflet was determined by the Ministry of Health and its content was checked and approved in July 2011.

OFLOXACINA
2 mg/ ml SOLUTION FOR INJECTION

PRESCRIBING INFORMATION

Ofloxacin hydrochloride
1 vial of solution for injection for IV perfusion contains 200 mg / 100 ml

COMPOSITION
Ofloxacin hydrochloride.....(*) 220 mg
(*) Equivalent to 200 mg of Ofloxacin
Sodium chloride
Hydrochloric acid (to adjust pH)
Water for injection

PHARMACEUTICAL FORM
Package with 1 or 10 vials of solution for injection for IV perfusion

PHARMACOTHERAPEUTIC GROUP: Antibiotic

NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER
FARMOZ-Sociedade Técnico Medicinal, S.A.
Rua da Tapada Grande, 2, Abrunheira
2710-089 Sintra
Portugal

THERAPEUTIC INDICATIONS
The use of 2mg/ml Ofloxacina SOLUTION FOR INJECTION is limited to adults with mild infections, caused by susceptible strains of microoganisms in the infections listed below.

- Respiratory tract infections;
- Acute, chronic and recurrent infections of the respiratory tract, including bronchitis and pneumonia;
- Chronic and recurring infections of the ORL tract (tonsillitis, pharyngitis, otitis and tracheitis);
- Septicaemia;
- Joint and bone infections;
- Skin and soft tissue infections;
- Abdomen infections;
- Kidney, genital-urinary tract infections, including gonorrhoea.

Ofloxacin anti-bacterial spectrum is the following:
Usually susceptible strains: (MIC $\leq$ 2 μg/ml): *Escherichia coli, Citrobacter, Proteus mirabilis, Proteus vulgaris, Klebsiella, Enterobacter, Salmonella, Shigella, Yersinia enterocolitica, Vibrio cholerae, Vibrio parahaemolyticus, Campylobacter jejuni, Campylobacter pylori, Aeromonas, Plesiomonas, Haemophilus influenzae and para-influenzae, Haemophilus ducreyi, Neisseria gonorrhoeae, Neisseria meningitidis, Branhamella catarrhalis, Legionella, Staphylococcus aureus, Staphylococcus epidermidis,Clostridium perfingens, Mycoplasma, Chlamydia:*
Strains not always susceptible: *Streptococcus and Pneumococcus, Enterococci, Listeria, Serratia marcescens, Pseudomonas aeruginosa, Gardnerella vaginalis, Cocos gram positive anaerobes, Mycobacterium tuberculosis, Ureaplasma urealyticulum:*
- Strains usually resistant: (MIC $\geq$ 8 μg/ml): *Bacteroides fragilis, Clostridium difficile, Nocardia asteroides.*

CONTRA-INDICATIONS

- Hypersensitivity to Ofloxacin or other quinolones;
- Epilepsy,past history of tendinitis;
- Children and adolescents;
- Pregnant women and women who have recently given birth, breast feeding women;
- Glucose – 6 – phosphate-dehydrogenise deficiency;
- As with all quinolones, ofloxacin may cause CNS stimulation, and is contra-indicated in patients with a known or suspected CNS disorder that may predispose to lower the seizure threshold;
- Fluoroquinolones, including Ofloxacina, may exacerbate muscle weakness in persons with myasthenia gravis. Avoid Ofloxacina in patients with known history of myasthenia gravis.

ADVERSE REACTIONS
2mg/ml OFLOXACINA SOLUTION FOR INJECTION is usually well tolerated and the adverse reactions of the product are similar to the other of the quinolones. There were reports of adverse reactions in 2 to 12% of the patients receiving Ofloxacin.

Gastrointestinal system: Nausea, abdominal pain, diarrhoea and vomiting.
Very rare: cholestatic jaundice, hepatitis or severe liver damage may develop. A particular form of enterocolitis that can occur with antibiotics is pseudomembranous colitis (in most cases due to *Clostridium difficile*). Even if *Clostridium difficile* is only suspected, administration of ofloxacin should be discontinued immediately, and appropriate treatment given. Drugs that inhibit peristalsis should not be administered in such cases

Nervous system: Headaches, insomnia, dizziness, sleep disorders and visual disturbances. Very rarely (less than 1% of the patients) anxiety, depression, hallucinations, unsteady pace, tremors, convulsions and paresthesia. Hearing disorders.
Exacerbation of Myasthenia Gravis: fluoroquinolones like Ofloxacina may cause worsening of myasthenia gravis symptoms, including muscle weakness and breathing problems. Patients should call their healthcare provider right away if they have any worsening muscle weakness or breathing problems.

Hypersensitivity reactions: Rash and pruritus. There have been rare reports of photosensitivity in patients receiving Ofloxacin.
Genital-urinary system: Ofloxacin is not nephrotoxic. There have been rare reports of serum creatinine increase.
Hepatic: In very rare cases a mild and temporary increase of hepatic enzymes (AST and ALT) and bilirubinemia
Cardiovascular system: Very rarely temporary hypotension.
Rare: circulatory collapse (due to pronounced drop in blood pressure);
Musculoskeletal system: In very rare cases muscle and/or joint pains.
Haematopoietic: In very rare cases there have been changes on the blood formula. (Leucopoenia, thrombocytopenia, agranulocytosis and anemia).
In very rare cases, haemolytic anaemia may develop.
Renal side effects:
Rare: Disturbances of kidney function.
Isolated cases: Acute interstitial nephritis, or an increase in serum creatinine, which may progress to acute renal failure
Local injection site reactions: Pain and inflammatory signs; more rarely thrombophlebitis.
Other side effects:
Rare: Malaise.
Very rare: Excessive rise or fall in blood-sugar levels. Weakness, joint and muscle pains (in isolated cases these may be symptoms of rhabdomyolysis).
Isolated cases: Tendon discomfort, including inflammation and rupture of tendons (e.g. the Achilles tendon) particularly in patients treated concurrently with corticosteroids. In the event of signs of inflammation of a tendon, treatment with Tarivid must be halted immediately and appropriate treatment must be initiated for the affected tendon.
The possibility cannot be ruled out that ofloxacin may trigger an attack of porphyria in predisposed patients. Except in very rare instances (e.g. isolated cases of smell, taste and hearing disorders) the adverse effects observed subsided after discontinuation of ofloxacin

INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION
In patients treated antivitamin K (oral anticoagulant) surveillance is required.
Ofloxacin might increase serum theophyline levels, although less than other quinolones.
Further lowering of the cerebral seizure threshold may also occur with certain nonsteroidal anti-inflammatory drugs.

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).
Interactions with laboratory tests: Determination of opiates or porphyrins in urine may give false-positive results during treatment with ofloxacin.
Concurrent administration of OFLOXACINA 2mg/ml SOLUTION FOR INJECTION with hypotensive medicaments might cause abrupt hypotension. In these cases and also with narcotic or barbiturate medicaments, the cardiovascular function should be monitored.

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE In patients with impaired renal function, adjustment in dosage is necessary, as Ofloxacin is eliminated primarily by renal excretion. (See POSOLOGY)
The occurrence of severe and persistent diarrhoea might be a symptom of a pseudomembranous colitis. After the diagnosis of pseudomembranous colitis has been established, although rare, treatment must be immediately discontinued and a specific antibiotic (vancomicin) must be used. In this case the administration of anti-peristaltic drugs should be avoided.
Although the majority of Ofloxacin hypersensitivity reactions are moderate skin reactions, there have been reports of severe hypersensitivity reactions and in cases fatal, some times following the first dose. The drug should be discontinued immediately at the first appearance of rash or any other sign of hypersensitivity.
Excessive sunlight should be avoided during treatment due to photosensitivity risk.
As Streptococcus and Pneumococcus are not always sensitive to Ofloxacin, the medicament must not be prescribed as a drug of first choice for nosocomials respiratory infections, except when there is a precise bacteriological study.
During treatment of infections by Pseudomonas aeruginosa and Staphylococcus aureus the occurrence of resistant mutants is described, and association with other antibiotic might be needed.
If neurological adverse reactions occur, observed in some cases right after first dose, physician must be informed.
Fluoroquinolones, including Ofloxacina, have neuromuscular blocking activity and may exacerbate muscle weakness in persons with myasthenia gravis. Postmarketing serious adverse events, including deaths and requirement for ventilatory support, have been associated with fluoroquinolone use in persons with myasthenia gravis. Avoid Ofloxacina in patients with known history of myasthenia gravis.

PREGNANCY AND LACTATION
The safety of OFLOXACINA 2mg/ml SOLUTION FOR INJECTION in pregnant women and lactating women has not been established, thus it is contra-indicated.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
In some patients, OFLOXACINA 2mg/ml SOLUTION FOR INJECTION might affect the capacity of reaction, in order to interfere with the capacity to drive or handle machines. This effect is increased by the ingestion of alcoholic drinks.

LIST OF EXCIPIENTS
Sodium chloride, hydrochloric acid and water for injections.

POSOLOGY AND METHOD OF ADMINISTRATION
Adult
In patients with normal renal function:
Urinary tract infections: 1 X 100 mg to 200 mg / day
Kidney and genital infections: 2 X 100 mg to 200 mg/day with a 12 hour interval
Respiratory tract infections: 2 X 200 mg/day with a 12 hour interval
Bone and joint infections: 2 X 200 mg/day with a 12 hour interval
Skin and soft tissue infections: 2 X 200 mg/day with a 12 hour interval
Abdominal infections: 2 X 200 mg/day with a 12 hour interval
Septicaemia: 2 X 200 mg/day with a 12 hour interval
In cases of pathogenic agents with variable sensitivity, severe respiratory infections, complicated infections or insufficient response to the medicament, the dose might be adjusted to 2 X 400 mg/day, 2 X 200 mg/day with a 12 hour interval.

In patients with impaired renal function:
The first administration is the same as recommended for patients with normal renal function. After this first administration, dosage should be adjusted as follows:
Moderate renal impairment (20-50 ml/minute clearance): 1 X 100 mg to 200 mg/day
Severe renal impairment (< 20 ml/min creatinine clearance): 1 X 100 mg/each two days
Dosage might be doubled, if necessary.
In patients with renal impairment and in patients undergoing haemodialysis, Ofloxacin levels in serum should be monitorized.

Method of Administration
OFLOXACINA SOLUTION FOR INJECTION is presented as a solution ready- to-use and is only for IV administration. The solution should be administrated during 30 minutes.

Compatibilities
OFLOXACINA SOLUTION FOR INJECTION must not be administered simultaneously with other solutions for which compatibility is not proved. OFLOXACINA is compatible with the following solutions: 0.9% sodium chloride, 5% glucose, 5% fructose and Ringer solution.

Duration of treatment
The duration of the therapy depends on the type and severity of the infection and it must be determined by the clinical and bacteriological response of the patient.
As with other antibiotics, it is essential to continue with the therapy for at least 3 days after the disappearance of signs and symptoms of infection. For the majority of severe infections, a 7 to 10 days treatment is sufficient.
In infections due to beta-haemolytic streptococcus, treatment shall continue for at least 10 days.
In the total, treatment with OFLOXACINA INJECTION treatment must not exceed 2 months.
Oral therapy with the same dosage regimen might be carried out after patients' improvement.

MEASURES IN CASE A DOSE IS MISSED
Patient must comply with the prescribed therapeutic, respecting the antibiotic administration timings, without missing any dose.
In case you miss one dose, restart to take it and adjust timings, in accordance with the last administration.

OVERDOSE
In case of overdose, the treatment is symptomatic and of support.
In case of severe adverse reactions after overdose, haemodialysis or peritoneal dialysis might increase medicament elimination (although only small quantities are eliminated) mainly in patients with compromised renal function.

WARNINGS
In case of undesirable effects non-indicated in this leaflet, inform your physician or pharmacist.
Do not use OFLOXACINA SOLUTION FOR INJECTION after expiring the shelf life indicated in package. After opening of OFLOXACINA SOLUTION FOR INJECTION vial, the product must be immediately used.
Medicament subjected to prescription

SPECIAL PRECAUTIONS FOR STORAGE
OFLOXACINA must be stored at room temperature, under 25ºC and protected from sunlight.

MANUFACTURER
B. BRAUN Medical S.A
SPAIN
For:
FARMOZ – Sociedade Tecnico Medicinal, S.A.
PORTUGAL

REGISTRATION OWNER
BioAvenir Ltd
Kibutz Glil Yam 46905

Product : Ofloxacina Israel

code: PL Ofloxacina PB0813-01

Laetus: N/A

Size: 130x420 mm

Fold (nº): N/A

Color1: Black

Paper Ior (gr/m2): 50/60

1st proof: 10 oct 2013 **Author:** Marco Medeiros