Ladinin®

CIPROFLOXACIN

PATIENT INFORMATION LEAFLET

1. DESCRIPTION OF THE MEDICINAL PRODUCT

1.1 NAME: LADININ

1.2 COMPOSITION

Active ingredient: Ciprofloxacin

•250mg/tab, 500mg/tab: *Excipients:* Starch maize, cellulose microcrystalline, crospovidone, precipitated silica, magnesium stearate.

Film coating: Hypromellose, Macrogol 400, Titanium Dioxide CI 77891 E171.

•100mg/50ml Vial, 200mg/100ml Vial: *Excipients:* Lactic acid (90%), sodium chloride, hydrochloric acid (1N) to pH 3.5 - 4.6, water for injections.

1.3 PHARMACEUTICAL DOSAGE FORM

•Film Coated Tablets. •Solution for injection for intravenous infusion.

1.4 STRENGTH OF THE ACTIVE INGREDIENT

•250mg/tab, 500mg/tab. •100mg/50ml Vial, 200mg/100ml Vial.

1.5 DESCRIPTION-PACKAGING

•250mg/tab, 500mg/tab: A cardboard box containing a blister cartridge of transparent PVC/Aluminium with 10 tablets and is accompanied by an information leaflet.

•100mg/50ml (vial): A cardboard box containing a glass vial of 50ml sealed by a rubber stopper and alumium cap and is accompanied by an information leaflet.

•200mg/100ml (vial): A cardboard box containing a glass vial of 100ml sealed by a rubber stopper and aluminium cap and is accompanied by an information leaflet.

1.6 THERAPEUTIC CATEGORY: Antibiotic.

1.7 MARKETING AUTHORIZATION HOLDER

Pharmathen S.A., 6, Dervenakion Str., Pallini, Attica, Greece, Tel.: +30.210.6665067, Fax: +30.210.6666749.

1.8 MANUFACTURER

Pharmathen S.A., 6, Dervenakion Str., Pallini, Attica, Greece, Tel.: +30.210.6665067, Fax: +30.210.6666749.

2. WHAT YOU SHOULD KNOW ABOUT THE MEDICINE YOUR DOCTOR HAS PRESCRIBED

2.1 General Information

Ladinin, contains ciprofloxacin which is a member of the quinolone class of antibiotics, appropriate for the treatment of infections.

2.2 Indications

Ladinin is indicated for the treatment of infections caused by susceptible strains of the named microorganisms in the conditions listed below:

Lower respiratory tract infections

Oral or parenteral administration

Caused by *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Proteus mirabilis, Pseudomonas aeruginosa.* Not effective in pneumococcal pneumonia.

Ciprofloxacin is especially effective against *Pseudomonas aeruginosa* in cystic fibrosis.

Prevention of the development of inhalation anthrax following possible or known bacillus anthracis spore inhalation.

Skin & soft tissue

Oral or parenteral administration

Caused by *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Proteus mirabilis, Proteus vulgaris, Providencia stuartii, Morganella morganii, Citrobacter freundii, Pseudomonas aeruginosa, Staphylococcus aureus* and *Staphylococcus epidermidis* (methicilin) resistant strains. A combination with another antibiotic (e.g. rifampicin), in order to prevent the development of ciprofloxacin resistance is recommended, in the latter case.

Bone and joint infections

Oral or parenteral administration

Caused specifically by *Enterobacter cloacae, Serratia marcescens, Pseudomonas aeruginosa* as well as by enterobacteria in general.

Urinary tract infections

Oral or parenteral administration

• Infections of the upper urinary tract caused by *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Serratia marcescens, Proteus mirabilis, Providencia rettgeri, Morganella morganii, Citrobacter diversus, Citrobacter freundii, Pseudomonas aeruginosa.*

• Infections of the lower urinary tract e.g. chronic prostatitis, chronic and recurrent cystitis caused by gram-negative organisms resistant to penicillins and cefalosporines e.g. *E. Coli, Klebsiella pneumoniae, Enterobacter cloacae, Serratia marcescens, Proteus mirabilis, Providencia rettgeri, Morganella morganii, Citrobacter diversus, Citrobacter freundii, Pseudomonas aeruginosa.*

• Infections of the genital organs. Ciprofloxacin is effective for the treatment of soft ulcers. Gonococcal infections caused from resistant gonococcal strains.

Gastro-intestinal infections

In gastroenteritis caused by *Salmonella typhi, Shigella spp, Campylobacter spp* and traveller's diarrhoea.

Parenteral

Intra-abdominal infections caused by multi-resistant gram-negative microorganisms in combination with an antibacterial with anaerobic action.

Septicaemia, Endocarditis

Oral or parenteral administration

By gram-negative nosocomeial multi-resistant pathogen strains. Endocarditis by Q fever *(Coxiella burnetti).*

Prophylactic treatment for CNS infections caused by *N. Meningitides.*

2.3 Contraindications

Ladinin is contraindicated in persons with a history of hypersensitivity to ciprofloxacin or any other member of the quinolone class.

Not to be administered to patients with a history of tendon alterations, a history of tendonitis or tendon rupture.

Administration to children and adolescents is contraindicated. Exacerbations of cystic fibrosis and prevention of inhalation anthrax development is an exception (see children).

Ciprofloxacin should not be administered during pregnancy or breast-feeding as there is not enough experience regarding the drug's safety in this patient group.

2.4 SPECIAL WARNINGS AND PRECAUTIONS

2.4.1 General

As with all the other fluoroquinolones, incidents of tendonitis, usually regarding the Achilles tendon, which may cause tendon rupture, have been reported. In the case of tendonitis, treatment should be discontinued, the patient should be completely immobilized and the doctor's advice should be requested. Factors that predispose to tendonitis are: age above 60, intense physical exercise and long-term treatment with corticosteroids, as well as the initial recovery period in patients, who have been bedridden for a substantial time period. Patients should be warned for the possibility of pain in the Achilles tendon (pain in the ankle and heel area).

Cystic fibrosis in pediatric patients

Analysis of the available safety data regarding the administration to children or adolescents less than 18 years of age, who suffered from cystic fibrosis, has shown no correlation to the cartilage and joints erosions.

Clinical and pharmacokinetic data are available for the support of ciprofloxacin's administration to children with cystic fibrosis, for the treatment of acute respiratory exacerbation caused by *P. aeruginosa.* However, its use in other diseases besides cystic fibrosis is contraindicated.

Pseudomembranous colitis has been reported with nearly all antibacterial agents. For this reason, in patients who present diarrhoea related to the drug's use, the possibility of pseudomembranous colitis development should be examined. Colitis may be mild, severe or even life threatening. Mild cases usually respond to simple drug discontinuation. Moderate or severe cases require appropriate measures to be instituted.

2.4.2 Elderly patients: Although in the case of elderly patients, higher levels of ciprofloxacin are found in the blood serum, dosage adjustment is not necessary.

Elderly patients should be treated at the minimum dose depending on severity of the disease and creatinine clearance.

2.4.3 Pregnancy: Contraindicated.

2.4.4 Breast-feeding: Contraindicated.

2.4.5 Children: As with other drugs of this group, ciprofloxacin has been shown to cause arthropathy of weight-bearing joints in immature animals. Although the significance of this phenomenon for humans is unknown, its use in children and adolescents during the age of maturity is contraindicated.

Exceptions are exacerbations of cystic fibrosis and the prevention of inhalation anthrax development (see Dosage).

2.4.6 Effects on the ability to drive and use machines: The administration of the drug may effect the reaction time to such a degree that the ability to drive or use machines may be affected. This occurs particularly in conjuction with alcohol.

2.4.7 Special warnings for the excipients: Do not take Ladinin if you are allergic to any of its excipients.

2.5 Interactions with other medicines or substances

Concurrent administration of ciprofloxacin with theophylline may result in increased risk of theophylline-related adverse reactions. If concomitant use cannot be avoided, plasma levels of theophylline should be monitored and relevant dosage adjustments made.

In concurrent ciprofloxacin administration (orally) with iron, sucralfate, didanocin, antacids and drugs containing magnesium, aluminium and calcium, ciprofloxacin should be administered 1-2 hours before or at least 4 hours after the administration of these preparations. This restriction does not apply to H_2 receptors' antagonists.

Probenecid interferes with urinary tube secretion of ciprofloxacin and produces an increase in ciprofloxacin plasma levels. This should be considered if patients are receiving both drugs concomitantly.

Azlocilline administered intravenously produces an increase of ciprofloxacin concentrations.

As with other broad spectrum antibiotics, the prolonged use of ciprofloxacin may result in an excessive development of non sensitive microorganisms. Repeated evaluation of the patient's condition and microbial susceptibility testing is essential. If superinfection occurs during treatment, appropriate measures should be taken.

The combination of quinolones with certain non-steroidal anti-inflammatory drugs (besides acetylsalicylic acid) may produce convulsions. The same has been reported in combination with foscarnet.

Concurrent administration of ciprofloxacin with orally administered anticoagulants may enforce the latter's pharmacological actions.

When ciprofloxacin is administered concurrently with cyclosporine, it is necessary to regularly check the serum creatinine levels of these patients (twice a week).

There are also indications of synergic nephrotoxicity in concurrent administration with cyclosporine.

In some cases, concurrent administration of ciprofloxacin and glibenclamide may intensify the latter's action (hypoglycaemia).

Opiates should not be administered during the perioperative period to patients receiving ciprofloxacin.

Metoclopramide accelerates ciprofloxacin's absorption, resulting in a decrease of the time period of the maximum plasma concentrations, with no effect on bioavailability. Concurrent administration with methotrexate, may result in higher levels of plasma methotrexate and may increase its toxicity. For this reason, patients under treatment with methotrexate should be closely monitored in case that they should be treated concurrently with ciprofloxacin.

2.6 Dosage and administration

Tablets

The usual dosage for patients with urinary tract infections is 250mg to every 12 hours. For patients suffering from complicated urinary infections and infections of the upper urinary tract, 500mg every 12 hours could be administered.

Infections of the respiratory system, of the skin and skin formations, bones and joints, could be treated with 500mg every 12 hours. For more severe or complicated infections e.g. infections from *P. aeruginosa,* 750mg every 12 hours can be administered.

Dosage guidelines

Infection localization	Type or severity	Unit dose	Frequency	Daily dose
Urinary tract	Mild/Moderate	250 mg	Every 12 hours	500 mg
	Severe/Complicated	500 mg	Every 12 hours	1000 mg
Respiratory tract	Mild/Moderate	500 mg	Every 12 hours	1000 mg
Cystic fibrosis	See end of dosage			
Prevention of Anthrax		500 mg	Every 12 hours	1000 mg
Prevention of Meningitis		500 mg	Single dose	500 mg
Severe gastroenteritis		500 mg	Every 12 hours	1000 mg
Traveller'diarrhoea	Mild non dysenteric	750 mg	Single dose	750 mg
	Severe dysenteric	500 mg	Every 12 hours for 3 days	1000 mg
Intraabdominal infections		500 mg	Every 12 hours	1000 mg
Bones/Joints	Severe/Complicated	750 mg	Every 12 hours	1500 mg
Skin and skin formations	Severe/Complicated	750 mg	Every 12 hours	1500 mg

For the prevention of anthrax, administration of the medicine should be started as soon as possible after suspected of known inhalation.

Prevention of the development of inhalation anthrax following suspected of known inhalation of anthrax bacillus spores.

For this indication the risk-benefit assessment has shown that the administration of ciprofloxacin in children with the following dosage is suitable:

15mg/kg body weight twice a day. The maximum of 500mg per dose (maximum daily dose 1000mg) should not be exceeded.

The administration of the drug should be commenced as soon as possible after suspected or known inhalation.

The total duration of preventative therapy is 60 days.

Intravenous infusion

General dosage administrations: Dosage of intravenous ciprofloxacin is determined by the severity and type of the infection, the sensitivity of the responsible microbial factor (or microbes) and the age, weight and renal function of the patient.

Adults

In patients with cystic fibrosis, ciprofloxacin has been shown to create photosensitivity reactions, in rare cases. For this reason, these patients are recommended to avoid excessive exposure to direct sunlight during the treatment with ciprofloxacin. However, if this is not possible, the patient should use sunblock cream.

Precautions

General

As with quinolones, ciprofloxacin may cause stimulation of the central nervous system (CNS) that may result in tremor, anxiety, lightheadedness and very rarely hallucinations or convulsions. For this reason, ciprofloxacin should be used with caution in patients with known or suspected CNS disorders, such as severe cerebral arteriosclerosis or epilepsy, or in the presence of other factors that predispose to convulsions (see "Adverse effects").

Caution should be taken in hepatic or renal function disorders, G6PD deficiency or myasthenia gravis.

Exposure to direct sunlight and radiation should be avoided.

Crystallouria related to ciprofloxacin has been reported only rarely in humans because human urine is usually acidic. Patients administered with ciprofloxacin should be well hydrated and urine alkalination should be avoided.

The daily-recommended dose should not be exceeded.

Alteration of the dose regimen is necessary in patients with renal function disorders (see "Dose and Administration").

Dosage guidelines for adults are: 100mg-200mg twice daily. However, in septic as well as in neutropenic patients or patients with systemic infections caused by *Pseudomonas aeruginosa*, a dosage of 200-400mg/ 8 hours is possible and should be administered.

For infections of the lower and upper urinary tracts, 100-200mg twice daily.

In case of infections of the respiratory system, 200-400mg twice daily, for both upper and lower respiratory tract infections.

For the prevention of anthrax, 400mg are administered intravenous twice daily. The drug's administration for this indication should begin as soon as possible after the suspected or known inhalation.

For the majority of the rest of the infections, 200mg twice daily should be administered, with precaution to infections caused by *P. aeruginosa*, where dosage should be higher.

Dosage Adjustments

Elimination of ciprofloxacin occurs primarily by the kidney, however it is also metabolised and partially excreted through the biliary route of the liver and also eliminated from the intestinal tract. The alternative routes of elimination compensate impaired renal function. Therefore, dosage adjustments are usually not required, apart from in the following circumstances.

1. **Reduced renal function**
   Creatinine clearance < 20ml/min or serum creatinine levels > 3mg/100ml. Total daily dose is reduced to 50% per 24 hours.
2. **Reduced renal function and haemodialysis**
   Dose as above. On dialysis days, dose administration should occur after the haemodialysis.

3. Reduced hepatic function

No adjustment of dosage is required.

4. Reduced renal and hepatic function

Normal dose every 24 hours of reduction of the dose by 50%, if necessary. Monitoring of drug serum levels is recommended.

Treatment duration

Tablets: The treatment duration depends on the severity of the infection. Generally, ciprofloxacin should be continued for at least 3 days after the disappearance of the symptoms and signs of the infection.

The usual duration is 7-14 days, unless otherwise defined in the above table.

However, severe and complicated infections, may require more extended treatment.

Bone and joint infections may require a treatment duration of 4 to 6 weeks, or even more.

For the indication of the prevention of anthrax, total duration of preventative treatment is 60 days.

For the indication of cystic fibrosis, the recommended duration of treatment is 10-14 days.

Renal function reduction

The following table provides the dosage to be used for patients with renal damage. Yet, the most trustworthy base for the dosage determination is the constant measurement of the drug's levels in the blood serum.

Recommended initial doses and maintenance doses for patients suffering from reduced renal function

Creatinine clearance (ml/min)	Dosage
> 50	See usual dosage
30-50	250-500 mg/12h
5-29	250-500 mg/18h
Patients with haemodialysis or peritoneal dialysis (after dialysis)	250-500 mg/24h

When only the serum creatinine density is known, the following equation can be used for the calculation of creatinine.

$$\text{Men: creatinine clearance} = \frac{\text{Body weight (kg)} \times (140 - \text{age})}{72 \times \text{serum creatinine (mg/dl)}}$$

Women: 0,85 x the value calculated for men.

The creatinine value should represent a steady state of the renal function. In patients with severe infections and severe reduction of renal function, a dose of 750mg, every 18 hours, or 24 hours (see table). Those patients, however, should be closely monitored and ciprofloxacin plasma levels should be periodically measured. Peak values (1-2 hours after the administration) exceeding 50mcg/ml should be avoided.

In cases of patients with renal function in a stage of change, or patients with reduced renal function and hepatic failure, the blood serum ciprofloxacin density measurement will offer additional help for the dosage regulation.

Reduced hepatic function

No dosage adjustment is required.

Intravenous infusion: Treatment duration depends on the infection's severity, the clinical response and the microbiological findings.

For acute infections the usual treatment period is 5-7 days. In general, the treatment should be continued for at least 3 days following the disappearance of the infection signs and symptoms.

For the indication of anthrax prevention, the total treatment duration is 60 days.

For the indication of cystic fibrosis, the recommended treatment duration is 10-14 days.

The initial intravenous administration may be followed by oral treatment with ciprofloxacin.

Oral and parenteral administration

Tablets: the tablets are swallowed whole with a small amount of liquid. They may be taken independently of meals. When the tablets are taken on an empty stomach the active ingredient is absorbed more rapidly. When the patients are not able to take oral therapy, either due to the severity of the illness, or for other reasons, treatment should commence intravenously. Oral treatment may follow.

Intravenous infusion: ciprofloxacin should be administered in infusion of duration of more than 60 minutes. Slow infusion in a large vein minimizes discomfort by the patient and reduces the danger of phlevitis.

The solution for intravenous infusion may be infused either directly or after mixture with other compatible for infusion solutions.

Infusion vials of 50ml (100mg), 100ml (200mg) may be infused immediately.

The dosage of an individual patient should be determined, having first taken into consideration the severity and the nature of the infection, the sensitivity of the causal microbe, the integrity of the defense mechanism of the patient and the condition of the renal function.

Oral and parenteral

Elderly patients

Although in elderly patients higher levels of blood serum ciprofloxacin are found, dosage adjustment is not necessary.

Elderly patients should be treated with the minimum dose depending on the severity of the disease and the creatinine clearance.

Adolescents and children

As with other drugs of its group, ciprofloxacin has been proved to produce arthropathy in weight-bearing joints of immature animals. Although the significance of this phenomenon for humans is unknown, its use in children and adolescents in the age of development is contraindicated.

Exacerbations of cystic fibrosis and the prevention of inhalation anthrax development is an exception (see below).

Cystic fibrosis

In adults with infection of the lower respiratory tracts caused by pseudomonas, the dosage is that for infections caused by *P. aeruginosa*.

In children with cystic fibrosis (aged 5-17) with acute respiratory exacerbation, oral administration of 20mg/kg of bodyweight twice daily is indicated (maximum dosage 1500mg daily) or 10mg/kg of bodyweight intravenously every 8 hours (maximum daily dosage 1200mg). The infusion should be administered in a time period of more than 60 minutes.

The dosage in children with impaired renal and hepatic function has not been studied.

2.7 Overdosage - Treatment

In cases of acute, excessive oral overdosage, reversible renal toxicity has been reported. Therefore, it is recommended, besides usual emergency measures, to check the renal function and to administer antacids containing magnesium or calcium that reduce ciprofloxacin's absorption. Only a small amount of ciprofloxacin (< 10%) is excreted from the body after haemodialysis or peritoneal catharsis.

2.8 Side effects

Hepatic failure, renal failure, anaphylactic reactions, haemolysis and hypoglycaemia (especially during concurrent administration of glibenclamide) may appear during administration of quinolones, which, if not noticed by the attendant doctor or patient, may result in death. Moreover, tendonitis, especially of the Achilles tendon, which may result even in tendon rupture, may appear.

Patients receiving concurrently coumarin anticoagulant should be carefully observed because there is a possibility of increase in the anticoagulant action beyond the predicted one.

Topical irritation (concerns only the solution for injection) with pain at the infusion site accompanied in a small number of patients by phlevitis or thrombophlevitis.

Topical reactions at the injection site have been reported following the intravenous administration of ciprofloxacin. These reactions appear more often, if the time of infusion is 30 minutes or less. They may appear as topical skin reactions, which disappear right after the injection. Intravenous administration is therefore not contraindicated unless the reactions continue or worsen.

Ciprofloxacin is in general well tolerated. During a clinical study, 2799 patients received 2868 series of the drug. Side effects that were considered to possible be related to the drug appeared in 7.3% of the series, to be possibly related to the drug in 9.2% of the series and to be impossibly related in 3%. Ciprofloxacin was discontinued due to side effects in 3.5% of the series. They regarded mostly the gastrointestinal system (1.5%), the skin (0.6%) and the central nervous system (0.4%).

The most common reported incidents, related or not to the drug, were nausea (5.2%), diarrhoea (2.3%), vomiting (2.2%), pain-discomfort in the abdominal area (1.7%), headaches (1.2%), anxiety (1.1%) and rash (1.1%).

Listed below are the adverse effects observed per organ. Those typical for quinolones appear in italics.

Gastrointestinal

Nausea, diarrhoea, vomiting, dyspepsia, abdominal pain, flatulence, anorexia.

In case of a severe form of diarrhoea during or after the treatment's discontinuation, the patient should be examined by a doctor because severe intestinal disorder (pseudomembranous colitis) may be latent. In these cases, ciprofloxacin should be discontinued and the proper treatment should be administered (e.g. vancomycin), orally, 4 x 250mg /daily. Drugs that prevent peristalsis are prohibited.

Rarely the following have appeared: painful mucosal stomatitis. oral candidiasis, dysphagia, intestine perforation, and gastrointestinal haemorrhage.

Central nervous system

Dizziness, headaches, feeling of fatigue, anxiety, tremor. Rarely: *lightheadedness, perspiration, walking instability, insomnia, nightmares, hallucination, manic reaction, hyperexcitability, ataxia, convulsions, lethargy, somnolence, weakness, indisposition, anorexia, phobia, depersonification, depression, delusions, increase of intra-cranial pressure, stress, confusion, peripheral painful sensation.*

Some times these reactions appear following the administration of the first dose. In these cases, ciprofloxacin administration should be discontinued and the patient should be examined by a doctor.

Skin / Hypersensitivity

In some cases, the following reactions appear following the administration of ciprofloxacin. In these cases, drug administration should be discontinued and the doctor should be notified.

Skin reactions e.g. *rash, itching, pharmoceutical fever.*

Rarely: Petechia, formation of haemorrhagic blisters (haemorrhagic bullae) and small tumors (papulae) with the formation of crusts that indicates vascular attack (vasculitis), skin hyperpigmentation, oedematous erythema, multiforme erythema, skin candidiasis, flushing, photosensitivity.

Stevens-Johnson syndrome, Lyell syndrome.

Intermediate nephritis, hepatitis, hepatic necrosis that very rarely gradually evolves into life threatening hepatic failure.

Anaphylactic reactions (*e.g. oedema of the face, neck, lips, conjunctivae or hands, oedema of the larynx, angioedema, dyspnea that gradually evolves in life threatening shock, urticaria*) that in some cases appear following the administration of ciprofloxacin for the first time.

In these cases, ciprofloxacin administration should be discontinued and an appropriate therapeutic treatment should be recommended by a doctor.

Special senses

Rarely the following are observed: *blurred vision, disturbed vision (change in colour perception, overbrightness of lights), decreased visual acuity, diplopia, eye pain, tinnitus, hearing disturbance, mostly regarding high frequencies, bad taste, bad olfaction.*

Musculoskeletal

Rarely *arthrolgia or back pain, joint stiffness, joints oedema, neck or chest pain, flare up of gout, muscular pains, tenosynovitis.*

In isolated cases, during the administration of ciprofloxacin, Achilles tendon tendonitis was observed.

In isolated cases, partial or total rupture of the Achilles tendon was reported, mostly in elderly patients with prior systematic administration of glycocorticoids. For this reason, if Achilles tendon rupture is suspected (painful oedema), ciprofloxacin administration should be discontinued and the doctor should be notified.

Renal / Genitourinary

Rarely: Interstitial nephritis, nephritis, renal failure, polyuria, urinary retention, vaginitis, urethral bleeding, acidosis.

Cardiovascular

Palpitation and rarely ventricular flutter, ventricular ectopy, syncope, hypertension, angina pectoris, myocardic infarction, cardiopulmonary arrest, cerebral thrombosis, migraines, fainting.

Respiratory

Rarely: Epistaxis, laryngeal or pulmonary oedema, hiccough, haemoptysis, dyspnea, bronchospasm, pulmonary embolism.

Most of these incidents were described as mild or moderate in severity, abated soon after the drug was discontinued and required no treatment.

In several instances nausea, vomiting , tremor, irritability, agitation or the feeling of palpitations were judged by investigators to be related to elevated serum plasma levels of theophylline, possibly as a result of drug interaction with ciprofloxacin.

Prolonged or repeated administration of ciprofloxacin may result in superinfection with resistant bacteria or fungi.

Adverse effects during laboratory examinations

Changes in laboratory parameters listed as side effects without correlation to the drug.

Hepatic: Elevations of SGPT (ALT) (1.9%), SGOT (AST) (1.7%), alkaline phosphatase (0.8%), LDH (0.4%), serum bilirubin (0.3%).

Haematological: Eosinophilia (0.6%), leukopenia (0.4%), agranulocytosis, decreased blood platelets (0.1%), elevated blood platelets (0.1%), pancytopenia (0.1%).

Renal: Elevations of serum creatinine (1.1%), BUN (0.9%), crystalluria, cylindruria and haematuria have been reported. Other changes occurring in rare occasions were: elevation of γ-GT, elevation of serum amylase, reduction of blood glycose, elevated uric acid, decrease in haemoglobin, anaemia, haemorrhagic disposition, increase in large monocytes in blood, leukocytosis, haemolytic anaemia, changes in prothrombin time.

2.9 What the patient should do in case of a missed dose

If you miss a dose, you should replace it as soon as possible, unless the time of the next dose is near. Continue your treatment normally, as indicated by your doctor.

Do not double your doses.

2.10 Expiry date of the medicinal product

The expiry date is printed on the external and internal packaging.

If this date has already passed, do not take the medicine.

2.11 Special precautions for storage of the medicinal product

Solution for intravenous infusion: Because ciprofloxacin presents photosensitivity, the vials should not be removed from the outer package before use. The solution for injection must be protected from excessive heat and not be frozen.

By follow ing the correct pharmaceutical practice, each solution must be used within 24 hours from its preparation.

Tablets: Store in a cool and dry place at temperature 15 - 25° C. Protect from light. Keep out of the reach and sight of children.

2.12 Instructions for use and handling

Solution for intravenous infusion: 100mg/50ml, 200mg/100ml may be infused immediately and should be administered in small infusion periods over 30 - 60 minutes.

2.13 Date of last revision of the text

Prot. No.: 10825/20-3-2002

3. INFORMATION REGARDING THE CORRECT USE OF DRUGS

This medicine has been prescribed for you by your doctor only for your specific medical condition. You should not give it to other people or use it for a different condition, without first consulting your doctor. •If during treatment a problem regarding the drug occurs, immediately notify your doctor or pharmacist. •If there are any questions regarding the information related to the drug you receive or if you need to be better informed about your medical condition, do not hesitate to ask your doctor or pharmacist. •In order for the drug prescribed to you to be effective and safe, it should be taken according to the given instructions. •For your health and safety, it is necessary to read carefully all information related to the drug. •Do not keep drugs in bathroom cupboards because heat and moisture may alter the drug and make it harmful for your health. •Do not keep drugs you no longer require or that have expired. •For greater safety, keep all drugs in a safe place and out of the reach and sight of children.