1.3 Summary Product Characteristics (SPC)

1. Name of the medicinal product

CIPROFLOXACIN TABLETS BP 500MG

2. Qualitative and quantitative composition

Each Film coated tablet contains:
Ciprofloxacin hydrochloride BP
Eq. to Ciprofloxacin ..... 500 mg
Excipients ..... QS
Color: Titanium dioxide BP

3. Pharmaceutical form

Tablet.

A white coloured, oblong shaped, biconvex, film coated tablet, bisected on one side.

4. Clinical particulars

4.1 Therapeutic indications

Ciprofloxacin tablets used in following infection:
Adults
• Lower respiratory tract infections due to Gram-negative bacteria
  - exacerbations of chronic obstructive pulmonary disease
  - broncho-pulmonary infections in cystic fibrosis or in bronchiectasis
  - pneumonia
• Chronic suppurative otitis media
• Acute exacerbation of chronic sinusitis especially if these are caused by Gram-negative bacteria
• Urinary tract infections
• Genital tract infections
  - gonococcal uretritis and cervicitis due to susceptible Neisseria gonorrhoeae
  - epididymo-orchitis including cases due to susceptible Neisseria gonorrhoeae
  - pelvic inflammatory disease including cases due to susceptible Neisseria gonorrhoeae
• Infections of the gastro-intestinal tract (e.g. travellers' diarrhoea)
• Intra-abdominal infections
• Infections of the skin and soft tissue caused by Gram-negative bacteria
• Malignant external otitis
• Infections of the bones and joints
• Prophylaxis of invasive infections due to Neisseria meningitidis
• Inhalation anthrax (post-exposure prophylaxis and curative treatment)

Ciprofloxacin may be used in the management of neutropenic patients with fever that is suspected to be due to a bacterial infection.

Children and adolescents

• Broncho-pulmonary infections in cystic fibrosis caused by Pseudomonas aeruginosa
• Complicated urinary tract infections and pyelonephritis

• Inhalation anthrax (post-exposure prophylaxis and curative treatment)
Ciprofloxacin may also be used to treat severe infections in children and adolescents when this is considered to be necessary.
Treatment should be initiated only by physicians who are experienced in the treatment of cystic fibrosis and/or severe infections in children and adolescents

4.2 Posology and method of administration

The dosage is determined by the indication, the severity and the site of the infection, the susceptibility to ciprofloxacin of the causative organism(s), the renal function of the patient and, in children and adolescents the body weight.
The duration of treatment depends on the severity of the illness and on the clinical and bacteriological course.
Treatment of infections due to certain bacteria (e.g. *Pseudomonas aeruginosa*, *Acinetobacter* or *Staphylococci*) may require higher ciprofloxacin doses and co-administration with other appropriate antibacterial agents.
Treatment of some infections (e.g. pelvic inflammatory disease, intra-abdominal infections, infections in neutropenic patients and infections of bones and joints) may require co-administration with other appropriate antibacterial agents depending on the pathogens involved.
Adults

Indications		**Daily dose in mg**	**Total duration of treatment (potentially including initial parenteral treatment with ciprofloxacin)**
Infections of the lower respiratory tract		500 mg twice daily to 750 mg twice daily	7 to 14 days
Infections of the upper respiratory tract	Acute exacerbation of chronic sinusitis	500 mg twice daily to 750 mg twice daily	7 to 14 days
	Chronic suppurative otitis media	500 mg twice daily to 750 mg twice daily	7 to 14 days
	Malignant external otitis	750 mg twice daily	28 days up to 3 months
Urinary tract infections (see section 4.4)	Uncomplicated cystitis	250 mg twice daily to 500 mg twice daily	3 days
		In pre-menopausal women, 500 mg single dose may be used	
	Complicated cystitis, Uncomplicated pyelonephritis	500 mg twice daily	7 days
	Complicated pyelonephritis	500 mg twice daily to 750 mg twice daily	at least 10 days, it can be continued for longer than 21 days in some specific circumstances (such as abscesses)
	Prostatitis	500 mg twice daily to 750 mg twice daily	2 to 4 weeks (acute) to 4 to 6 weeks (chronic)

Genital tract infections	Gonococcal uretritis and cervicitis	500 mg as a single dose	1 day (single dose)
	Epididymo-orchitis and pelvic inflammatory diseases	500 mg twice daily to 750 mg twice daily	at least 14 days
Infections of the gastro-intestinal tract and intra-abdominal infections	Diarrhoea caused by bacterial pathogens including *Shigella* spp. other than *Shigella dysenteriae* type 1 and empirical treatment of severe travellers' diarrhoea	500 mg twice daily	1 day
	Diarrhoea caused by *Shigella dysenteriae* type 1	500 mg twice daily	5 days
	Diarrhoea caused by *Vibrio cholerae*	500 mg twice daily	3 days
	Typhoid fever	500 mg twice daily	7 days
	Intra-abdominal infections due to Gram-negative bacteria	500 mg twice daily to 750 mg twice daily	5 to 14 days
Infections of the skin and soft tissue		500 mg twice daily to 750 mg twice daily	7 to 14 days
Bone and joint infections		500 mg twice daily to 750 mg twice daily	max. of 3 months
Neutropenic patients with fever suspected to be due to a bacterial infection. Ciprofloxacin should be co-administered with appropriate antibacterial agent(s) in accordance to official guidance.		500 mg twice daily to 750 mg twice daily	Therapy should be continued over the entire period of neutropenia
Prophylaxis of invasive infections due to *Neisseria meningitidis*		500 mg as a single dose	1 day (single dose)
Inhalation anthrax post-exposure prophylaxis and curative treatment for persons able to receive treatment by oral route when clinically appropriate. Drug administration should begin as soon as possible after suspected or confirmed exposure.		500 mg twice daily	60 days from the confirmation of *Bacillus anthracis* exposure

Paediatric population

Indications	**Daily dose in mg**	**Total duration of treatment (potentially including initial parenteral treatment with ciprofloxacin)**

Cystic fibrosis	20 mg/kg body weight twice daily with a maximum of 750 mg per dose.	10 to 14 days
Complicated urinary tract infections and pyelonephritis	10 mg/kg body weight twice daily to 20 mg/kg body weight twice daily with a maximum of 750 mg per dose.	10 to 21 days
Inhalation anthrax post-exposure prophylaxis and curative treatment for persons able to receive treatment by oral route when clinically appropriate. Drug administration should begin as soon as possible after suspected or confirmed exposure.	10 mg/kg body weight twice daily to 15 mg/kg body weight twice daily with a maximum of 500 mg per dose.	60 days from the confirmation of *Bacillus anthracis* exposure
Other severe infections	20 mg/kg body weight twice daily with a maximum of 750 mg per dose.	According to the type of infections

Elderly patients
Elderly patients should receive a dose selected according to the severity of the infection and the patient's creatinine clearance.

Patients with renal and hepatic impairment
Recommended starting and maintenance doses for patients with impaired renal function:

Creatinine Clearance [mL/min/1.73 m^2]	**Serum Creatinine [µmol/L]**	**Oral Dose [mg]**
> 60	< 124	See Usual Dosage.
30-60	124 to 168	250-500 mg every 12 h
< 30	> 169	250-500 mg every 24 h
Patients on haemodialysis	> 169	250-500 mg every 24 h (after dialysis)
Patients on peritoneal dialysis	> 169	250-500 mg every 24 h

In patients with impaired liver function no dose adjustment is required.
Dosing in children with impaired renal and/or hepatic function has not been studied.

Method of administration
Tablets are to be swallowed unchewed with fluid. They can be taken independent of mealtimes. If taken on an empty stomach, the active substance is absorbed more rapidly. Ciprofloxacin tablets should not be taken with dairy products (e.g. milk, yoghurt) or mineral-fortified fruit-juice (e.g. calcium-fortified orange juice) .
In severe cases or if the patient is unable to take tablets (e.g. patients on enteral nutrition), it is recommended to commence therapy with intravenous ciprofloxacin until a switch to oral administration is possible.

4.3 Contraindications

- Hypersensitivity to the active substance, to other quinolones or to any of the excipients
- • Concomitant administration of ciprofloxacin and tizanidine

4.4 Special warnings and precautions for use

Severe infections and mixed infections with Gram-positive and anaerobic pathogens
Ciprofloxacin monotherapy is not suited for treatment of severe infections and infections that might be due to Gram-positive or anaerobic pathogens. In such infections ciprofloxacin must be co-administered with other appropriate antibacterial agents.
Streptococcal Infections (including Streptococcus pneumoniae)
Ciprofloxacin is not recommended for the treatment of streptococcal infections due to inadequate efficacy.
Genital tract infections
Gonococcal uretritis, cervicitis, epididymo-orchitis and pelvic inflammatory diseases may be caused by fluoroquinolone-resistant *Neisseria gonorrhoeae* isolates.
Therefore, ciprofloxacin should be administered for the treatment of gonococcal uretritis or cervicitis only if ciprofloxacin-resistant *Neisseria gonorrhoeae* can be excluded.
For epididymo-orchitis and pelvic inflammatory diseases, empirical ciprofloxacin should only be considered in combination with another appropriate antibacterial agent (e.g. a cephalosporin) unless ciprofloxacin-resistant *Neisseria gonorrhoeae* can be excluded. If clinical improvement is not achieved after 3 days of treatment, the therapy should be reconsidered.
Urinary tract infections
Resistance to fluoroquinolones of *Escherichia 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 *Escherichia coli* to fluoroquinolones.
The single dose of ciprofloxacin, that may be used in uncomplicated cystitis in pre-menopausal women, is expected to be associated with lower efficacy than the longer treatment duration. This is all the more to be taken into account as regards the increasing resistance level of *Escherichia coli* to quinolones.
Intra-abdominal infections
There are limited data on the efficacy of ciprofloxacin in the treatment of post-surgical intra-abdominal infections.
Travellers' diarrhoea
The choice of ciprofloxacin should take into account information on resistance to ciprofloxacin in relevant pathogens in the countries visited.
Infections of the bones and joints
Ciprofloxacin should be used in combination with other antimicrobial agents depending on the results of the microbiological documentation.
Inhalational anthrax
Use in humans is based on *in-vitro* susceptibility data and on animal experimental data together with limited human data. Treating physicians should refer to national and/or international consensus documents regarding the treatment of anthrax.
Paediatric population

The use of ciprofloxacin in children and adolescents should follow available official guidance. Ciprofloxacin treatment should be initiated only by physicians who are experienced in the treatment of cystic fibrosis and/or severe infections in children and adolescents.

Ciprofloxacin has been shown to cause arthropathy in weight-bearing joints of immature animals. Safety data from a randomised double-blind study on ciprofloxacin use in children

(ciprofloxacin: n=335, mean age = 6.3 years; comparators: n=349, mean age = 6.2 years; age range = 1 to 17 years) revealed an incidence of suspected drug-related arthropathy (discerned from joint-related clinical signs and symptoms) by Day +42 of 7.2% and 4.6%. Respectively, an incidence of drug-related arthropathy by 1-year follow-up was 9.0% and 5.7%. The increase of suspected drug-related arthropathy cases over time was not statistically significant between groups. Treatment should be initiated only after a careful benefit/risk evaluation, due to possible adverse events related to joints and/or surrounding tissue

Broncho-pulmonary infections in cystic fibrosis

Clinical trials have included children and adolescents aged 5-17 years. More limited experience is available in treating children between 1 and 5 years of age.

Complicated urinary tract infections and pyelonephritis

Ciprofloxacin treatment of urinary tract infections should be considered when other treatments cannot be used, and should be based on the results of the microbiological documentation.

Clinical trials have included children and adolescents aged 1-17 years.

Other specific severe infections

Other severe infections in accordance with official guidance, or after careful benefit-risk evaluation when other treatments cannot be used, or after failure to conventional therapy and when the microbiological documentation can justify a ciprofloxacin use.

The use of ciprofloxacin for specific severe infections other than those mentioned above has not been evaluated in clinical trials and the clinical experience is limited. Consequently, caution is advised when treating patients with these infections.

Hypersensitivity

Hypersensitivity and allergic reactions, including anaphylaxis and anaphylactoid reactions, may occur following a single dose and may be life-threatening. If such reaction occurs, ciprofloxacin should be discontinued and an adequate medical treatment is required.

Musculoskeletal System

Ciprofloxacin should generally not be used in patients with a history of tendon disease/disorder related to quinolone treatment. Nevertheless, in very rare instances, after microbiological documentation of the causative organism and evaluation of the risk/benefit balance, ciprofloxacin may be prescribed to these patients for the treatment of certain severe infections, particularly in the event of failure of the standard therapy or bacterial resistance, where the microbiological data may justify the use of ciprofloxacin.

Tendinitis and tendon rupture (especially Achilles tendon), sometimes bilateral, may occur with ciprofloxacin, even within the first 48 hours of treatment. Inflammation and ruptures of tendon may occur even up to several months after discontinuation of ciprofloxacin therapy. The risk of tendinopathy may be increased in elderly patients or in patients concomitantly treated with corticosteroids

At any sign of tendinitis (e.g. painful swelling, inflammation), ciprofloxacin treatment should be discontinued. Care should be taken to keep the affected limb at rest.

Ciprofloxacin should be used with caution in patients with myasthenia gravis, because symptoms can be exacerbated

Vision disorders

If vision becomes impaired or any effects on the eyes are experienced, an eye specialist should be consulted immediately.

Photosensitivity

Ciprofloxacin has been shown to cause photosensitivity reactions. Patients taking ciprofloxacin should be advised to avoid direct exposure to either extensive sunlight or UV irradiation during treatment

Central Nervous System

Ciprofloxacin like other quinolones are known to trigger seizures or lower the seizure threshold. Cases of status epilepticus have been reported. Ciprofloxacin should be used with caution in patients with CNS disorders which may be predisposed to seizure. If seizures occur ciprofloxacin should be discontinued Psychiatric reactions may occur even after first

administration of ciprofloxacin. In rare cases, depression or psychosis can progress to suicidal ideations/thoughts culminating in attempted suicide or completed suicide. In the occurrence of such cases, ciprofloxacin should be discontinued.
Cases of polyneuropathy (based on neurological symptoms such as pain, burning, sensory disturbances or muscle weakness, alone or in combination) have been reported in patients receiving ciprofloxacin. Ciprofloxacin should be discontinued in patients experiencing symptoms of neuropathy, including pain, burning, tingling, numbness, and/or weakness in order to prevent the development of an irreversible condition

Cardiac disorders

Caution should be taken when using fluoroquinolones, including ciprofloxacin, 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 ciprofloxacin, in these populations.

Hypoglycemia

As with other quinolones, hypoglycemia has been reported most often in diabetic patients, predominantly in the elderly population. In all diabetic patients, careful monitoring of blood glucose is

Gastrointestinal System

The occurrence of severe and persistent diarrhoea during or after treatment (including several weeks after treatment) may indicate an antibiotic-associated colitis (life-threatening with possible fatal outcome), requiring immediate treatment (see section 4.8). In such cases, ciprofloxacin should immediately be discontinued, and an appropriate therapy initiated. Anti-peristaltic drugs are contraindicated in this situation.

Renal and urinary system

Crystalluria related to the use of ciprofloxacin has been reported Patients receiving ciprofloxacin should be well hydrated and excessive alkalinity of the urine should be avoided.

Impaired renal function

Since ciprofloxacin is largely excreted unchanged via renal pathway dose adjustment is needed in patients with impaired renal function as to avoid an increase in adverse drug reactions due to accumulation of ciprofloxacin.

Hepatobiliary system

Cases of hepatic necrosis and life-threatening hepatic failure have been reported with ciprofloxacin In the event of any signs and symptoms of hepatic disease (such as anorexia, jaundice, dark urine, pruritus, or tender abdomen), treatment should be discontinued.

Glucose-6-phosphate dehydrogenase deficiency

Haemolytic reactions have been reported with ciprofloxacin in patients with glucose-6-phosphate dehydrogenase deficiency. Ciprofloxacin should be avoided in these patients unless the potential benefit is considered to outweigh the possible risk. In this case, potential occurrence of haemolysis should be monitored.

Resistance

During or following a course of treatment with ciprofloxacin bacteria that demonstrate resistance to ciprofloxacin may be isolated, with or without a clinically apparent superinfection. There may be a particular risk of selecting for ciprofloxacin-resistant bacteria during extended durations of treatment and when treating nosocomial infections and/or infections caused by *Staphylococcus* and *Pseudomonas* species.

Cytochrome P450

Ciprofloxacin inhibits CYP1A2 and thus may cause increased serum concentration of concomitantly administered substances metabolised by this enzyme (e.g. theophylline,

clozapine, olanzapine, ropinirole, tizanidine, duloxetine, agomelatine). Therefore, patients taking these substances concomitantly with ciprofloxacin should be monitored closely for clinical signs of overdose, and determination of serum concentrations (e.g. of theophylline) may be necessary Co-administration of ciprofloxacin and tizanidine is contra-indicated.
Methotrexate
The concomitant use of ciprofloxacin with methotrexate is not recommended Interaction with tests
The *in-vitro* activity of ciprofloxacin against *Mycobacterium tuberculosis* might give false negative bacteriological test results in specimens from patients currently taking ciprofloxacin.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of other products on ciprofloxacin:
Drugs known to prolong QT interval
Ciprofloxacin, like other fluoroquinolones, should be used with caution in patients receiving drugs known to prolong QT interval (e.g. Class IA and III anti-arrhythmics, tricyclic antidepressants, macrolides, antipsychotics)
Chelation Complex Formation
The simultaneous administration of ciprofloxacin (oral) and multivalent cation-containing drugs and mineral supplements (e.g. calcium, magnesium, aluminium, iron), polymeric phosphate binders (e.g. sevelamer or lanthanum carbonate), sucralfate or antacids, and highly buffered drugs (e.g. didanosine tablets) containing magnesium, aluminium, or calcium reduces the absorption of ciprofloxacin. Consequently, ciprofloxacin should be administered either 1-2 hours before or at least 4 hours after these preparations. The restriction does not apply to antacids belonging to the class of H2 receptor blockers.
Food and Dairy Products
Dietary calcium as part of a meal does not significantly affect absorption. However, the concurrent administration of dairy products or mineral-fortified drinks alone (e.g. milk, yoghurt, calcium-fortified orange juice) with ciprofloxacin should be avoided because absorption of ciprofloxacin may be reduced.
Probenecid
Probenecid interferes with renal secretion of ciprofloxacin. Co-administration of probenecid and ciprofloxacin increases ciprofloxacin serum concentrations.
Metoclopramide
Metoclopramide accelerates the absorption of ciprofloxacin (oral) resulting in a shorter time to reach maximum plasma concentrations. No effect was seen on the bioavailability of ciprofloxacin.
Omeprazole
Concomitant administration of ciprofloxacin and omeprazole containing medicinal products results in a slight reduction of C_{max} and AUC of ciprofloxacin.
Effects of ciprofloxacin on other medicinal products:
Tizanidine
Tizanidine must not be administered together with ciprofloxacin. In a clinical study with healthy subjects, there was an increase in serum tizanidine concentration (C_{max} increase: 7-fold, range: 4 to 21-fold; AUC increase: 10-fold, range: 6 to 24-fold) when given concomitantly with ciprofloxacin. Increased serum tizanidine concentration is associated with a potentiated hypotensive and sedative effect.
Methotrexate
Renal tubular transport of methotrexate may be inhibited by concomitant administration of ciprofloxacin, potentially leading to increased plasma levels of methotrexate and increased risk of methotrexate-associated toxic reactions. The concomitant use is not recommended
Theophylline
Concurrent administration of ciprofloxacin and theophylline can cause an undesirable increase in serum theophylline concentration. This can lead to theophylline-induced side

effects that may rarely be life threatening or fatal. During the combination, serum theophylline concentrations should be checked and the theophylline dose reduced as necessary

Other xanthine derivatives

On concurrent administration of ciprofloxacin and caffeine or pentoxifylline (oxpentifylline), raised serum concentrations of these xanthine derivatives were reported.

Phenytoin

Simultaneous administration of ciprofloxacin and phenytoin may result in increased or reduced serum levels of phenytoin such that monitoring of drug levels is recommended.

Cyclosporin

A transient rise in the concentration of serum creatinine was observed when ciprofloxacin and cyclosporin containing medicinal products were administered simultaneously. Therefore, it is frequently (twice a week) necessary to control the serum creatinine concentrations in these patients.

Vitamin K antagonists

Simultaneous administration of ciprofloxacin with a vitamin K antagonist may augment its anti-coagulant effects. The risk may vary with the underlying infection, age and general status of the patient so that the contribution of ciprofloxacin to the increase in INR (international normalised ratio) is difficult to assess. The INR should be monitored frequently during and shortly after co-administration of ciprofloxacin with a vitamin K antagonist (e.g., warfarin, acenocoumarol, phenprocoumon, or fluindione).

Duloxetine

In clinical studies, it was demonstrated that concomitant use of duloxetine with strong inhibitors of the CYP450 1A2 isozyme such as fluvoxamine, may result in an increase of AUC and C_{max} of duloxetine. Although no clinical data are available on a possible interaction with ciprofloxacin, similar effects can be expected upon concomitant administration

Ropinirole

It was shown in a clinical study that concomitant use of ropinirole with ciprofloxacin, a moderate inhibitor of the CYP450 1A2 isozyme, results in an increase of C_{max} and AUC of ropinirole by 60% and 84%, respectively. Monitoring of ropinirole-related side effects and dose adjustment as appropriate is recommended during and shortly after co-administration with ciprofloxacin

Lidocaine

It was demonstrated in healthy subjects that concomitant use of lidocaine containing medicinal products with ciprofloxacin, a moderate inhibitor of CYP450 1A2 isozyme, reduces clearance of intravenous lidocaine by 22%. Although lidocaine treatment was well tolerated, a possible interaction with ciprofloxacin associated with side effects may occur upon concomitant administration.

Clozapine

Following concomitant administration of 250 mg ciprofloxacin with clozapine for 7 days, serum concentrations of clozapine and N-desmethylclozapine were increased by 29% and 31%, respectively. Clinical surveillance and appropriate adjustment of clozapine dosage during and shortly after co-administration with ciprofloxacin are advised

Sildenafil

C_{max} and AUC of sildenafil were increased approximately twofold in healthy subjects after an oral dose of 50 mg given concomitantly with 500 mg ciprofloxacin. Therefore, caution should be used prescribing ciprofloxacin concomitantly with sildenafil taking into consideration the risks and the benefits.

Agomelatine

In clinical studies, it was demonstrated that fluvoxamine, as a strong inhibitor of the CYP450 1A2 isoenzyme, markedly inhibits the metabolism of agomelatine resulting in a 60-fold increase of agomelatine exposure. Although no clinical data are available for a possible interaction with ciprofloxacin, a moderate inhibitor of CYP450 1A2, similar effects can be expected upon concomitant administration

Zolpidem
Co-administration of ciprofloxacin may increase blood levels of zolpidem, concurrent use is not recommended.

4.6 Fertility, pregnancy and lactation

Pregnancy
The data that are available on administration of ciprofloxacin to pregnant women indicates no malformative or feto/neonatal toxicity of ciprofloxacin. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. In juvenile and prenatal animals exposed to quinolones, effects on immature cartilage have been observed, thus, it cannot be excluded that the drug could cause damage to articular cartilage in the human immature organism / foetus
As a precautionary measure, it is preferable to avoid the use of ciprofloxacin during pregnancy.
Breast-feeding
Ciprofloxacin is excreted in breast milk. Due to the potential risk of articular damage, ciprofloxacin should not be used during breast-feeding.

4.7 Effects on ability to drive and use machines

Due to its neurological effects, ciprofloxacin may affect reaction time. Thus, the ability to drive or to operate machinery may be impaired.

4.8 Undesirable effects

The most commonly reported adverse drug reactions (ADRs) are nausea and diarrhoea.

ADRs derived from clinical studies and post-marketing surveillance with Ciproxin (oral, intravenous, and sequential therapy) sorted by categories of frequency are listed below. The frequency analysis takes into account data from both oral and intravenous administration of ciprofloxacin.

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	**Frequency not known** (cannot be estimated from the available data)
Infections and Infestations		Mycotic superinfections			
Blood and Lymphatic System Disorders		Eosinophilia	Leukopenia Anaemia Neutropenia Leukocytosis Thrombocytopenia Thrombocytaemia	Haemolytic anaemia Agranulocytosis Pancytopenia (life-threatening) Bone marrow depression (life-threatening)	

Immune System Disorders			Allergic reaction Allergic oedema / angiooedema	Anaphylactic reaction Anaphylactic shock (life-threatening) Serum sickness-like reaction	
Metabolism and Nutrition Disorders		Decreased appetite	Hyperglycaemia Hypoglycaemia		
Psychiatric Disorders		Psychomotor hyperactivity / agitation	Confusion and disorientation Anxiety reaction Abnormal dreams Depression (potentially culminating in suicidal ideations/thoughts or suicide attempts and completed suicide) Hallucinations	Psychotic reactions (potentially culminating in suicidal ideations/thoughts or suicide attempts and completed suicide)	Mania, incl. hypomania
Nervous System Disorders		Headache Dizziness Sleep disorders Taste disorders	Par- and Dysaesthesia Hypoaesthesia Tremor Seizures (incl. status epilepticus Vertigo	Migraine Disturbed coordination Gait disturbance Olfactory nerve disorders Intracranial hypertension and seudotumor cerebri	Peripheral neuropathy and polyneuropathy
Eye Disorders			Visual disturbances (e.g. diplopia)	Visual colour distortions	
Ear and Labyrinth Disorders			Tinnitus Hearing loss / Hearing impaired		
Cardiac Disorders			Tachycardia		Ventricular arrhythmia and torsades de pointes (reported predominantly in patients with risk

					factors for QT prolongation), ECG QT prolonged
Vascular Disorders			Vasodilatation Hypotension Syncope	Vasculitis	
Respiratory, Thoracic and Mediastinal Disorders			Dyspnoea (including asthmatic condition)		
Gastrointestinal Disorders	Nausea Diarrhoea	Vomiting Gastrointestinal and abdominal pains Dyspepsia Flatulence	Antibiotic associated colitis (very rarely with possible fatal outcome)	Pancreatitis	
Hepatobiliary Disorders		Increase in transaminases Increased bilirubin	Hepatic impairment Cholestatic icterus Hepatitis	Liver necrosis (very rarely progressing to life-threatening hepatic failure) (	
Skin and Subcutaneous Tissue Disorders		Rash Pruritus Urticaria	Photosensitivity reactions	Petechiae Erythema multiforme Erythema nodosum Stevens-Johnson syndrome (potentially life-threatening) Toxic epidermal necrolysis (potentially life-threatening)	Acute Generalised Exanthematous Pustulosis (AGEP) Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
Musculoskeletal and Connective Tissue Disorders		Musculoskeletal pain (e.g. extremity pain, back pain, chest pain) Arthralgia	Myalgia Arthritis Increased muscle tone and cramping	Muscular weakness Tendinitis Tendon rupture (predominantly Achilles tendon) Exacerbation of symptoms of myasthenia gravis	

Renal and Urinary Disorders		Renal impairment	Renal failure Haematuria Crystalluria Tubulointerstitial nephritis		
General Disorders and Administration Site Conditions		Asthenia Fever	Oedema Sweating (hyperhidrosis)		
Investigations		Increase in blood alkaline phosphatase	Increased amylase		International normalised ratio increased (in patients treated with Vitamin K antagonists)

Paediatric population

The incidence of arthropathy (arthralgia, arthritis), mentioned above, is referring to data collected in studies with adults. In children, arthropathy is reported to occur commonly

4.9 Overdose

An overdose of 12 g has been reported to lead to mild symptoms of toxicity. An acute overdose of 16 g has been reported to cause acute renal failure.
Symptoms in overdose consist of dizziness, tremor, headache, tiredness, seizures, hallucinations, confusion, abdominal discomfort, renal and hepatic impairment as well as crystalluria and haematuria. Reversible renal toxicity has been reported.
Apart from routine emergency measures, e.g. ventricular emptying followed by medical carbon, it is recommended to monitor renal function, including urinary pH and acidify, if required, to prevent crystalluria. Patients should be kept well hydrated. Calcium or magnesium containing antacids may theoretically reduce the absorption of ciprofloxacin in overdoses.
Only a small quantity of ciprofloxacin (<10%) is eliminated by haemodialysis or peritoneal dialysis.
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: Fluoroquinolones, ATC code: J01MA02
Mechanism of action
As a fluoroquinolone antibacterial agent, the bactericidal action of ciprofloxacin results from the inhibition of both type II topoisomerase (DNA-gyrase) and topoisomerase IV, required for bacterial DNA replication, transcription, repair and recombination.
Pharmacokinetic/pharmacodynamic relationship

Efficacy mainly depends on the relation between the maximum concentration in serum (C_{max}) and the minimum inhibitory concentration (MIC) of ciprofloxacin for a bacterial pathogen and the relation between the area under the curve (AUC) and the MIC.

Mechanism of resistance

In-vitro resistance to ciprofloxacin can be acquired through a stepwise process by target site mutations in both DNA gyrase and topoisomerase IV. The degree of cross-resistance between ciprofloxacin and other fluoroquinolones that results is variable. Single mutations may not result in clinical resistance, but multiple mutations generally result in clinical resistance to many or all active substances within the class.

Impermeability and/or active substance efflux pump mechanisms of resistance may have a variable effect on susceptibility to fluoroquinolones, which depends on the physiochemical properties of the various active substances within the class and the affinity of transport systems for each active substance. All *in-vitro* mechanisms of resistance are commonly observed in clinical isolates. Resistance mechanisms that inactivate other antibiotics such as permeation barriers (common in *Pseudomonas aeruginosa*) and efflux mechanisms may affect susceptibility to ciprofloxacin.

Plasmid-mediated resistance encoded by qnr-genes has been reported.

Spectrum of antibacterial activity

Breakpoints separate susceptible strains from strains with intermediate susceptibility and the latter from resistant strains:

EUCAST Recommendations

Microorganisms	**Susceptible**	**Resistant**
Enterobacteriaceae	S ≤ 0.5 mg/L	R > 1 mg/L
Pseudomonas spp.	S ≤ 0.5 mg/L	R > 1 mg/L
Acinetobacter spp.	S ≤ 1 mg/L	R > 1 mg/L
Staphylococcus spp.[1]	S ≤ 1 mg/L	R > 1 mg/L
Haemophilus influenzae and *Moraxella catarrhalis*	S ≤ 0.5 mg/L	R > 0.5 mg/L
Neisseria gonorrhoeae	S ≤ 0.03 mg/L	R > 0.06 mg/L
Neisseria meningitidis	S ≤ 0.03 mg/L	R > 0.06 mg/L
Non-species-related breakpoints*	S ≤ 0.5 mg/L	R > 1 mg/L

1 *Staphylococcus* spp. - breakpoints for ciprofloxacin relate to high dose therapy.

* Non-species-related breakpoints have been determined mainly on the basis of PK/PD data and are independent of MIC distributions of specific species. They are for use only for species that have not been given a species-specific breakpoint and not for those species where susceptibility testing is not recommended.

The prevalence of acquired resistance may vary geographically and with 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.

Groupings of relevant species according to ciprofloxacin susceptibility

COMMONLY SUSCEPTIBLE SPECIES
Aerobic Gram-positive micro-organisms *Bacillus anthracis* (1)
Aerobic Gram-negative micro-organisms

Aeromonas spp. *Brucella* spp. *Citrobacter koseri* *Francisella tularensis* *Haemophilus ducreyi* *Haemophilus influenzae** *Legionella* spp. *Moraxella catarrhalis** *Neisseria meningitidis* *Pasteurella* spp. *Salmonella* spp.* *Shigella* spp.* *Vibrio* spp. *Yersinia pestis*
Anaerobic micro-organisms *Mobiluncus*
Other micro-organisms *Chlamydia trachomatis* ($) *Chlamydia pneumoniae* ($) *Mycoplasma hominis* ($) *Mycoplasma pneumoniae* ($)
SPECIES FOR WHICH ACQUIRED RESISTANCE MAY BE A PROBLEM
Aerobic Gram-positive micro-organisms *Enterococcus faecalis* ($) *Staphylococcus* spp.* (2)
Aerobic Gram-negative micro-organisms *Acinetobacter baumannii*[+] *Burkholderia cepacia*[+]* *Campylobacter* spp.[+]* *Citrobacter freundii** *Enterobacter aerogenes* *Enterobacter cloacae** *Escherichia coli** *Klebsiella oxytoca* *Klebsiella pneumoniae** *Morganella morganii** *Neisseria gonorrhoeae** *Proteus mirabilis** *Proteus vulgaris** *Providencia* spp. *Pseudomonas aeruginosa** *Pseudomonas fluorescens* *Serratia marcescens**
Anaerobic micro-organisms *Peptostreptococcus* spp. *Propionibacterium acnes*
INHERENTLY RESISTANT ORGANISMS
Aerobic Gram-positive micro-organisms *Actinomyces* *Enteroccus faecium*

Listeria monocytogenes
Aerobic Gram-negative micro-organisms *Stenotrophomonas maltophilia*
Anaerobic micro-organisms *Excepted as listed above*
Other micro-organisms *Mycoplasma genitalium* *Ureaplasma urealitycum*

* Clinical efficacy has been demonstrated for susceptible isolates in approved clinical indications
+ Resistance rate ≥ 50% in one or more EU countries
($): Natural intermediate susceptibility in the absence of acquired mechanism of resistance
(1): Studies have been conducted in experimental animal infections due to inhalations of *Bacillus anthracis* spores; these studies reveal that antibiotics starting early after exposition avoid the occurrence of the disease if the treatment is made up to the decrease of the number of spores in the organism under the infective dose. The recommended use in human subjects is based primarily on *in-vitro* susceptibility and on animal experimental data together with limited human data. Two-month treatment duration in adults with oral ciprofloxacin given at the following dose, 500 mg bid, is considered as effective to prevent anthrax infection in humans. The treating physician should refer to national and/or international consensus documents regarding treatment of anthrax.
(2): Methicillin-resistant *S. aureus* very commonly express co-resistance to fluoroquinolones. The rate of resistance to methicillin is around 20 to 50% among all staphylococcal species and is usually higher in nosocomial isolates.

5.2 Pharmacokinetic properties

Absorption
Following oral administration of single doses of 250 mg, 500 mg, and 750 mg of ciprofloxacin tablets, ciprofloxacin is absorbed rapidly and extensively, mainly from the small intestine, reaching maximum serum concentrations 1-2 hours later.
Single doses of 100-750 mg produced dose-dependent maximum serum concentrations (C_{max}) between 0.56 and 3.7 mg/L. Serum concentrations increase proportionately with doses up to 1000 mg.
The absolute bioavailability is approximately 70-80%.
A 500 mg oral dose given every 12 hours has been shown to produce an area under the serum concentration-time curve (AUC) equivalent to that produced by an intravenous infusion of 400 mg ciprofloxacin given over 60 minutes every 12 hours.
Distribution
Protein binding of ciprofloxacin is low (20-30%). Ciprofloxacin is present in plasma largely in a non-ionised form and has a large steady state distribution volume of 2-3 L/kg body weight. Ciprofloxacin reaches high concentrations in a variety of tissues such as lung (epithelial fluid, alveolar macrophages, biopsy tissue), sinuses, inflamed lesions (cantharides blister fluid), and the urogenital tract (urine, prostate, endometrium) where total concentrations exceeding those of plasma concentrations are reached.
Biotransformation
Low concentrations of four metabolites have been reported, which were identified as: desethyleneciprofloxacin (M 1), sulphociprofloxacin (M 2), oxociprofloxacin (M 3) and formylciprofloxacin (M 4). The metabolites display *in-vitro* antimicrobial activity but to a lower degree than the parent compound.
Ciprofloxacin is known to be a moderate inhibitor of the CYP 450 1A2 iso-enzymes.
Elimination

Ciprofloxacin is largely excreted unchanged both renally and, to a smaller extent, faecally. The serum elimination half-life in subjects with normal renal function is approximately 4-7 hours.

Excretion of ciprofloxacin (% of dose)		
	Oral Administration	
	Urine	**Faeces**
Ciprofloxacin	44.7	25.0
Metabolites (M_1-M_4)	11.3	7.5

Renal clearance is between 180-300 mL/kg/h and the total body clearance is between 480-600 mL/kg/h. Ciprofloxacin undergoes both glomerular filtration and tubular secretion. Severely impaired renal function leads to increased half lives of ciprofloxacin of up to 12 h. Non-renal clearance of ciprofloxacin is mainly due to active trans-intestinal secretion and metabolism. 1% of the dose is excreted via the biliary route. Ciprofloxacin is present in the bile in high concentrations.

Paediatric patients

The pharmacokinetic data in paediatric patients are limited.

In a study in children C_{max} and AUC were not age-dependent (above one year of age). No notable increase in C_{max} and AUC upon multiple dosing (10 mg/kg three times daily) was observed.

In 10 children with severe sepsis C_{max} was 6.1 mg/L (range 4.6-8.3 mg/L) after a 1-hour intravenous infusion of 10 mg/kg in children aged less than 1 year compared to 7.2 mg/L (range 4.7-11.8 mg/L) for children between 1 and 5 years of age. The AUC values were 17.4 mg*h/L (range 11.8-32.0 mg*h/L) and 16.5 mg*h/L (range 11.0-23.8 mg*h/L) in the respective age groups.

These values are within the range reported for adults at therapeutic doses. Based on population pharmacokinetic analysis of paediatric patients with various infections, the predicted mean half-life in children is approx. 4-5 hours and the bioavailability of the oral suspension ranges from 50 to 80%.

5.3 Preclinical safety data

Non-clinical data reveal no special hazards for humans based on conventional studies of single dose toxicity, repeated dose toxicity, carcinogenic potential, or toxicity to reproduction.

Like a number of other quinolones, ciprofloxacin is phototoxic in animals at clinically relevant exposure levels. Data on photomutagenicity/ photocarcinogenicity show a weak photomutagenic or phototumorigenic effect of ciprofloxacin *in-vitro* and in animal experiments. This effect was comparable to that of other gyrase inhibitors.

Articular tolerability

As reported for other gyrase inhibitors, ciprofloxacin causes damage to the large weight-bearing joints in immature animals. The extent of the cartilage damage varies according to age, species and dose; the damage can be reduced by taking the weight off the joints. Studies with mature animals (rat, dog) revealed no evidence of cartilage lesions. In a study in young beagle dogs, ciprofloxacin caused severe articular changes at therapeutic doses after two weeks of treatment, which were still observed after 5 months.

6. Pharmaceutical particulars

6.1 List of excipients

Collodial sillicon dioxide (aerosil) light

Starch (maize starch powder
Croscarmellose Sodium
Sodium benzoate
D.M.water
Talcum
Magnesium stearate
Potassium polacrillin
Cross povidone
Hydroxypropyl methyl cellulose
PEG-6000
Lactose
Titanium dioxide
Microcrystalline cellulose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

1 X 10 Tablets blister pack

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed off in accordance with local requirements.

1.3.3 PACKAGE INSERT

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

(CIPROFLOXACIN TABLETS BP 500 MG)

What is in this leaflet:

1. What are Ciprofloxacin tablets and what are they used for
2. What you need to know before you take Ciprofloxacin tablets
3. How to take Ciprofloxacin tablets
4. Possible side effects
5. How to store Ciprofloxacin tablets

1. What are Ciprofloxacin tablets and what are they used for

Ciprofloxacin belongs to a group of medicines known as the quinolone antibacterials, fluoroquinolones. It has high anti-bacterial activity against a wide range of organisms. Ciprofloxacin works by killing bacteria that cause infections. It only works with specific strains of bacteria. Adults:

Ciprofloxacin is used to treat the following bacterial infections: respiratory tract infections(e.g. certain types of pneumonia)

- long lasting or recurring ear or sinus infections
- urinary tract infections (bladder and kidneys infection)
- genital tract infections in men and women (e.g. gonorrhoea, a sexually transmitted
- disease) gastro-intestinal tract infections (e.g.severe gastro-enteritis) and intra-abdominal
- infections skin and soft tissue infections
- bone and joint infections
- to prevent infections due to the bacteria Neisseria meningitides which causes
- meningitis(brain and spinal cord inflammation) anthrax inhalation exposure (infection that occurs when the spores from bacteria Bacillus
- anthracis enters the body). Ciprofloxacin may be used in the management of patients with low white blood cell counts (neutropenia) who have a fever that is suspected to be due to a

bacterial infection. If you have a severe infection or one that is caused by more than one type of bacterium, you may be given additional antibiotic treatment in addition to Ciprofloxacin

Children and adolescents:

Ciprofloxacin should be used under specialist medical supervision, to treat the following bacterial infections for children and adolescents: lung and bronchial infections in children and adolescents suffering from cystic fibrosis

• (genetic disorder known to be an inherited disease of the secretory glands, including the glands that make mucus and sweat). complicated urinary tract infections, including infections that have reached the kidneys

• (pyelonephritis). anthrax inhalation exposure (infection that occurs when the spores from bacteria Bacillus

• anthracis enters the body). Ciprofloxacin may also be used to treat other specific severe infections in children and adolescents when your doctor considers this as necessary.

2. What you need to know before you take Ciprofloxacin tablets

Do not take Ciprofloxacin if you:

are allergic (hypersensitive) to the Ciprofloxacin, to any other quinolone drugs or to any of the other ingredients of Ciprofloxacin tablets (see section 6).

are taking tizanidine (see Section 2: Taking other medicines)

.• Warnings and precautions:

Talk to your doctor, pharmacist or nurse before taking Ciprofloxacin Tablets if:

you suffer from 'fits' or epilepsy or any other neurological conditions.

• you have ever had kidney problems because your treatment may need to be adjusted

• you have a history of tendon problems during previous treatment with antibiotics such as

• Ciprofloxacin you are diabetic because you may experience a risk of hypoglycaemia with ciprofloxacin.

• you have myasthenia gravis (a type of muscle weakness) because symptoms can be exacerbated. you or a member of your family is known to have a deficiency in glucose-6-phosphate

• dehydrogenase (G6PD), since you may experience a risk of anaemia with ciprofloxacin. If your eyesight becomes impaired or if your eyes seem to be otherwise affected, consult

• an eye specialist immediately

Heart problems

Caution should be taken when using this kind of medicine, if you were born with or have family history of prolonged QT interval (seen on ECG, electrical recording of the heart), have salt imbalance in the blood (especially low level of potassium or magnesium in the blood), have a very slow heart rhythm (called 'bradycardia'), have a weak heart (heart failure), have a history of heart attack (myocardial infarction), you are female or elderly or you are taking other medicines that result in abnormal ECG changes (see section Taking other medicines).

For the treatment of some genital tract infections, your doctor can prescribe another antibiotic in addition to ciprofloxacin. If there is no improvement in symptoms after 3 days of treatment, please consult your doctor.

Contact your doctor immediately, if any of the following occurs while taking Ciprofloxacin. Your doctor will decide whether treatment with Ciprofloxacin needs to be stopped.

Severe, sudden allergic reaction (an anaphylactic reaction/shock, angio-oedema). Even

with the first dose, there is a small chance that you may experience a severe allergic reaction with the following symptoms: tightness in the chest, feeling dizzy, sick or faint, or experiencing dizziness when standing up. If this happens, stop taking Ciprofloxacin tablets and contact your doctor immediately.

If your eyesight becomes impaired or if your eyes seem to be otherwise affected, consult an eye specialist immediately.

Pain and swelling in the joints and tendinitis may occur occasionally, particularly if you are elderly and are also being treated with corticosteroids. Inflammation and ruptures of tendons may occur even within the first 48 hours of treatment or up to several months after discontinuation of Ciprofloxacin tablets therapy. At the first sign of any pain or inflammation stop taking Ciprofloxacin tablets and rest the painful area. Avoid any unnecessary exercise, as this might increase the risk of a tendon rupture.

If you suffer from epilepsy or other neurological conditions such as cerebral ischemia or stroke, you may experience side effects associated with the central nervous system. If this happens, stop taking Ciprofloxacin tablets and contact your doctor immediately.

You may experience psychiatric reactions the first time you take Ciprofloxacin tablets.

• If you suffer from depression or psychosis, your symptoms may become worse under treatment with Ciprofloxacin tablets. In rare cases, depression or psychosis can progress to thoughts of suicide, suicide attempts, or completed suicide. If this happens, stop taking Ciprofloxacin tablets and contact your doctor immediately.

You may experience symptoms of neuropathy such as pain, burning, tingling, numbness and/or weakness. If this happens, stop taking Ciprofloxacin tablets and contact your doctor immediately.

Hypoglycemia has been reported most often in diabetic patients, predominantly in elderly population. If this happens, contact your doctor immediately.

Diarrhoea may develop while you are taking antibiotics, including Ciprofloxacin tablets, or even several weeks after you have stopped taking them. If it becomes severe or persistent or you notice that your stool contains blood or mucus, stop taking Ciprofloxacin tablets immediately, as this can be life-threatening. Do not take medicines that stop or slow down bowel movements and contact your doctor.

Tell the doctor or laboratory staff that you are taking Ciprofloxacin tablets if you have to provide a blood or urine sample.

If you suffer from kidney problems, tell the doctor because your dose may need to be adjusted. Ciprofloxacin tablets may cause liver damage. If you notice any symptoms such as loss of appetite, jaundice (yellowing of the skin), dark urine, itching, or tenderness of the stomach, stop taking Ciprofloxacin tablets and contact your doctor immediately. Ciprofloxacin tablets may cause a reduction in the number of white blood cells and your resistance to infection may be decreased. If you experience an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/pharynx/mouth or urinary problems you should see your doctor immediately. A blood test will be taken to check possible reduction of white blood cells (agranulocytosis). It is important to inform your doctor about your medicine.

Your skin becomes more sensitive to sunlight or ultraviolet (UV) light when taking Ciprofloxacin tablets. Avoid exposure to strong sunlight, or artificial UV light such as sunbeds.

Other medicines and Ciprofloxacin: Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including those medicines obtained without a

prescription. Ciprofloxacin can increase the level of the following substances in the blood: Agomelatine,

Zolpidem

• Do not take Ciprofloxacin together with tizanidine, because this may cause side effects such as low blood pressure and sleepiness (see Section 2: "Do not take Ciprofloxacin").

The following medicines are known to interact with Ciprofloxacin in your body. Taking Ciprofloxacin together with these medicines can influence the therapeutic effect of those medicines. It can also increase the probability of experiencing side effects.

Tell your doctor if you are taking:

Vitamin K antagonists (e.g. warfarin, acenocoumarol, phenprocoumon or fluindione) or other oral anti-coagulants (to thin the blood)

theophylline (for breathing problems)

- phenytoin (used to treat epilepsy)
- ropinirole (for Parkinson's disease)
- phenytoin (for epilepsy)
- cyclosporin (used to treat psoriasis, dermatitis, rheumatoid arthritis and in organ
- transplantation) probenecid (used to prevent gout)
- metoclopramide (used to treat nausea and vomiting (feeling/being sick) and migraine)
- ropinirole (used to treat Parkinson's disease)
- methotrexate (for certain types of cancer, psoriasis, rheumatoid arthritis)
- tizanidine (for muscle spasticity in multiple sclerosis)• clozapine (an antipsychotic)
- olanzapine (an antipsychotic)
- other medicines that can alter your heart rhythm: medicines that belong to the group of
- anti-arrhythmics (e.g. quinidine, hydroquinidine, disopyramide, amiodarone, sotalol, dofetilide, ibutilide), tricyclic antidepressants, some antimicrobials (that belong to the group

of macrolides), some antipsychotics. Ciprofloxacin may increase the levels of the following medicines in your blood: pentoxifylline (for circulatory disorders)

- caffeine• duloxetine (for depression, diabetic nerve damage or incontinence)
- lidocaine (for heart conditions or anesthetic use)
- sildenafil (e.g. for erectile dysfunction)

• Some medicines reduce the effect of Ciprofloxacin. Tell your doctor if you take or wish to take:

Antacids

•omeprazole mineral supplements

- sucralfate
- a polymeric phosphate binder (e.g. sevelamer or lanthanum carbonate)
- medicines or supplements containing calcium, magnesium, aluminium or iron

• If these preparations are essential, take Ciprofloxacin about two hours before or no sooner than four hours after them.

Taking Ciprofloxacin with food and drink

Unless you take Ciprofloxacin during meals, do not eat or drink any dairy products (such as milk or yogurt) or drinks with added calcium when you take the tablets. These can affect the absorption of ciprofloxacin and so you should take your tablets either 1 to 2 hours before or at least 4 hours after you have such products.

Pregnancy and breast-feeding

It is preferable to avoid the use of Ciprofloxacin during pregnancy.

Tell your doctor if you are pregnant or planning to become pregnant.

Do not take Ciprofloxacin tablets during breast feeding because ciprofloxacin is excreted in breast milk and can be harmful for your child. Ask your doctor or pharmacist for advice before taking any other medicine.

Driving and using machines

Ciprofloxacin may make you feel less alert. Some neurological adverse events can occur. Therefore, make sure you know how you react to ciprofloxacin before driving a vehicle or operating machinery. If in doubt, talk to your doctor. Important information about some of the ingredients of Ciprofloxacin tablets: Lactose monohydrate – If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Ciprofloxacin tablets

Always take ciprofloxacin tablets exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

a) Take the tablets exactly as your doctor has told you. The tablets should always be taken with plenty of water, as this will help to prevent the formation of tiny crystals in your urine (crystalluria).

b) Do not chew the tablets because they do not taste nice.

c) Do try to take the tablets at around the same time every day.

You can take the tablets at meal times or between meals. Any calcium you take as a part of a meal will not seriously affect uptake. However, do not take ciprofloxacin tablets with dairy products such as milk or yogurt or with fortified fruit juices (eg.Calcium-fortified orange juice).

Tell your doctor if you suffer from kidney problems because your dose may need to be adjusted. The treatment usually lasts from 5 to 21 days, but may take longer for severe infections.

Your dose will be dependent on the type and severity of your infection, your age, weight and kidney function. Your doctor will choose the best dose for you

If you take more Ciprofloxacin tablets than you should

If you take more than the prescribed dose, get medical help immediately. If possible, take your tablets or the box with you to show the doctor.

If you forget to take Ciprofloxacin tablets

If you forget to take a dose, take the normal dose as soon as you remember. If it is almost time for your next dose, do not take the missed dose and just carry on as before. Do not take a double dose to make up for a forgotten dose. Be sure to complete your course of treatment.

If you stop taking Ciprofloxacin tablets

It is important that you finish the course of treatment even if you begin to feel better after a few days. If you stop taking this medicine too soon your infection may not be completely cured and the symptoms of the infection may return or get worse. You might also develop resistance to the antibiotic.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, ciprofloxacin can cause side-effects, although not everybody gets them. You may suffer an allergic reaction, symptoms of which include rash, itching, difficulty in breathing or swelling of the face, lips, throat or tongue. If this happens to you, stop taking the tablets immediately and seek medical help.

STOP taking the tablets immediately and seek medical help if any of the following occur: muscle pain and/or weakness, inflammation of the joints and joint pain, increased

• muscle tone and cramping, inflammation of the tendons or tendon rupture, particularly affecting the large tendon at the back of the ankle (Achilles tendon). If you experience this, rest the affected limb, discontinue treatment and seek medical advice immediately. See section 2.

Unusual feelings of pain, burning, tingling, numbness or muscle weakness in the extremities (neuropathy)-See section 2.

infection with symptoms such as fever and serious deterioration of your general condition (there may be a dangerous drop in a type of white blood cells (agranulocytosis)

Severe allergic reactions manifested as various skin eruptions or rashes, breathing problem (for example, the potentially fatal anaphylactic reaction, Stevens-Johnson syndrome or toxic epidermal necrolysis),

Hypersensitivity reactions called DRESS drug reaction with eosinophilia and systemic symptoms such as Fever, severe rash, joint pain, enlarged lymph nodes and inflammation of one or more internal organs such as liver leading to abdominal pain, yellowing of the skin

and whites of the eyes and/or heart, lungs and kidneys; with changes to your blood counts, particularly white blood cells called eosinophils. See section 2.

Liver problems (eg. Jaundice –yellowing of skin and white part of eyes)- very rarely can lead to life-threatening liver failure

mental disturbances (psychotic reactions and depression potentially leading to• thoughts of suicide and suicide attempts), hallucinations (apparent perception of something not present)

inflammation of the bowel (colitis) which causes attacks of diarrhoea, sometimes containing blood and/or mucus) linked to antibiotic use (can be fatal in very rare cases)

blood or crystals in the urine, decreased urination (kidney failure)

• These are potentially serious side effects and you will need to seek urgent medical attention.

Other side effects are as below

Common: may affect up to 1 in 10 people

- nausea, diarrhoea

- joint pains in children

Uncommon: may affect up to 1 in 100 people

- fungal superinfections - a high concentration of eosinophils, a type of white blood cell

- decreased appetite - hyperactivity or agitation - headache, dizziness, sleeping problems, or taste disorders

- vomiting, abdominal pain, digestive problems such as stomach upset (indigestion/heartburn), or wind

- increased amounts of certain substances in the blood (transaminases and/or bilirubin)

- hives - poor kidney function - pains in your muscles and bones, feeling unwell (asthenia), or fever

- increase in blood alkaline phosphatase (a certain substance in the blood)

- Feeling highly excited (mania) or feeling great optimism and overactivity (hypomania),

Rare: may affect up to 1 in 1,000 people

- changes to the blood count (leukopenia, leukocytosis, neutropenia, anaemia), increased or decreased amounts of a blood clotting factor (thrombocytes)

- allergic reaction, swelling (oedema), or rapid swelling of the skin and mucous membranes (angio-oedema)

- increased blood sugar (hyperglycaemia)

- decreased blood sugar (hypoglycaemia) (see Section 2: Warnings and precautions)

- confusion, disorientation, anxiety reactions, strange dreams - tremors, seizures or giddiness - eyesight problems including double vision - tinnitus, loss of hearing, impaired hearing - rapid heartbeat (tachycardia)

- expansion of blood vessels (vasodilation), low blood pressure, or fainting

- shortness of breath, including asthmatic symptoms

- liver disorders, jaundice (cholestatic icterus), or hepatitis

- sensitivity to light (see Section 2: Warnings and precautions)

- urinary tract inflammation

- fluid retention or excessive sweating - increased levels of the enzyme amylase

Very rare: may affect up to 1 in 10,000 people

a special type of reduced red blood cell count (haemolytic anaemia); a drop in the number of red and white blood cells and platelets (pancytopenia), which may be fatal; and bone marrow depression, which may also be fatal (see Section 2: Warnings and precautions)

- allergic reaction known as serum sickness

- migraine, disturbed coordination, unsteady walk (gait disturbance), disorder of sense of smell (olfactory disorders), pressure on the brain (intracranial pressure and pseudotumor cerebri)

- visual colour distortions

- inflammation of the wall of the blood vessels (vasculitis)

- pancreatitis

- small, pin-point bleeding under the skin (petechiae);

Not known: frequency cannot be estimated from the available data

- abnormal fast heart rhythm, life-threatening irregular heart rhythm, alteration of the heart rhythm (called 'prolongation of QT interval', seen on ECG, electrical activity of the heart)

- pustular rash

- influence on blood clotting (in patients treated with Vitamin K antagonists)

- periods of overactive and excited behaviour

- Feeling highly excited (mania) or feeling great optimism and overactivity (hypomania), hypersensitivity reaction called DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms)

5. How to store Ciprofloxacin tablets C.

Store in the original package.°Do not store above 25 Keep out of the reach and sight of children. Do not use your tablets after the expiry date stated on the label or carton. Medicines should not be disposed of via waste water or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

STORAGE CONDITION

Store in a cool, dry place. Protect from light. Keep all medicines away from reach of children.

Packing and presentation:

1 x 10 BLISTER Pack

MANUFACTURED BY:

EUROLIFE HEALTHCARE PVT. LTD.