CIPROXIN®

Film-Coated Tablet

WARNING :
Fluoroquinolone are associated with an increased risk of tendonitis and tendon rupture in all ages. This risk is further increased in older patients usually over 60 years of age, in patient taking corticosteroid drug, and in patient with kidney, heart or lung transplants.

Important information, please read carefully!

Composition

Ciproxin® 500: 1 film-coated tablet contains 582 mg ciprofloxacin hydrochloride monohydrate, correspond to 500 mg ciprofloxacin.

Pharmacological Properties

Pharmacotherapeutic group: Fluoroquinolones
ATC Code: J01MA02

Ciprofloxacin is a new substance developed by Bayer AG belonging to the quinolone carboxylic acid group. The substance has a good bactericidal effect against a broad spectrum of bacteria.

Pharmacodinamic Properties
Mechanism of Action
The bactericidal action of ciprofloxacin results from inhibition of bacterial type II topoisomerases (DNA gyrase and topoisomerase IV), which are required for bacterial DNA replication, transcription, repair, and recombination.

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.

The bacterial genus and species listed below have been shown to commonly be susceptible to ciprofloxacin in vitro:

Aerobic Gram-positive Microorganisms
Bacillus anthracis
Streptococcus spp.

Aerobic Gram-negative Microorganisms

Aeromonas spp.	*Moraxella catarrhalis*
Brucella spp.	***Neisseria meningitidis***
Citrobacter koseri	*Pasteurella* spp.
Francisella tularensis	*Salmonella* spp.*
Haemophilus ducreyi	*Shigella* spp.
Haemophilius influenzae	***Vibrio* spp.**
***Legionella* spp.**	*Yersinia pestis*

Other Microorganisms
Chlamydia trachomatis
Chlamydia pneumoniae
Mycoplasma hominis

The following microorganisms for which acquired resistance may be a problem: *Acinetobacter baumann, Burkholderia cepacia, Campylobacter* spp., *Citrobacter freudii, Enterococcus faecalis, Enterobacter aerogenes, Enterobacter clocae,*

Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca, Mycoplasma genitalium, Morganella morganii, Neisseria gonorrhoeae, Proteus mirabilis, Proteus vulgaris, Providencia spp*., Pseudomonas aeruginosa, Pseudomonas fluorescens, Serratia marcescens, Streptococcus pneumoniae, Peptostreptococcus* spp
The following microorganisms are considered inherently resistant to ciprofloxacin: *Staphylococcus aureus* (methicillin-resistant), *Ureaplasma urealitycum*, Anaerobic microorganisms (Excepted *Peptostreptococus).*

Pharmacokinetic Properties
Absorption
Film coated tablet
Following oral administration of single doses of 250 mg, 500 mg, and 750 mg of ciprofloxacin film coated tablets ciprofloxacin is absorbed rapidly and extensively mainly from the small intestine, reaching maximum serum concentrations 1-2 hours later.
Mean Ciprofloxacin Serum Concentrations (mg/l)
after Oral Administration
[Time from tablet intake]

Time (h)	250 mg/L	500 mg/L	750 mg/L
0.5	0.9	1.7	2.9
1.0	1.3	2.5	3.5
2.0	0.9	2.0	2.9
4.0	0.5	1.3	1.7
8.0	0.3	0.6	0.8
12.0	0.2	0.4	0.5

The absolute bioavailability is approximately 70 - 80%. Maximum serum concentrations (C_{max}) and total areas under serum concentration vs. time curves (AUC) increased in proportion to dose.

Distribution
The protein binding of ciprofloxacin is low (20 - 30%), and the substance is present in plasma largely in a non-ionized form. Ciprofloxacin can diffuse freely into the extra-vascular space. The large steady-state volume of distribution of 2-3 l/kg body weight shows that ciprofloxacin penetrates in tissues resulting in concentrations which clearly exceed the corresponding serum levels.

Metabolism
Small concentrations of 4 metabolites have been reported. They were identified as desethyleneciprofloxacin (M 1), sulphociprofloxacin (M 2), oxociprofloxacin (M 3) and formylciprofloxacin (M 4). M 1 to M 3 display antibacterial activity comparable to or inferior to that of nalidixic acid. M 4, with the smallest quantity, is largely equivalent to norfloxacin in its antimicrobial activity.

Elimination
Ciprofloxacin is largely excreted unchanged both renally and, to a smaller extent, non-renally.
Excretion of Ciprofloxacin (% of dose)
Oral Administration

	Urine	**Faeces**
Ciprofloxacin	44.7	25.0
Metabolites (M_1-M_4)	11.3	7.5

Intravenous Administration

	Urine	**Faeces**
Ciprofloxacin	61.5	15.2
Metabolites (M_1-M_4)	9.5	2.6

Renal clearance is between 0.18-0.3 L/h/kg and the total body clearance between 0.48-0.60 L/h/kg. Ciprofloxacin undergoes both glomerular filtration and tubular secretion.
Non-renal clearance of ciprofloxacin is mainly due to active transintestinal secretion as well as metabolisation. 1% of the dose is via the biliary excreted route. Ciprofloxacin is present in the bile in high concentrations.

Children
In a study in children C_{max} and AUC were not age-dependent. No notable increase in C_{max} and AUC upon multiple dosing (10 mg/kg/TID) was observed. In 10 children with severe sepsis, less than 1 year of age C_{max} was 6.1 mg/L (range 4.6 – 8.3 mg/L) after a 1-hour intravenous infusion at a dose level of 10 mg/kg; and 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 pediatric patients with various infections, the predicted mean half-life in children is approx. 4 –5 hours and the bioavailability of the oral suspension approx. 60%.

Preclinical safety data

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Therapeutic indications

- Urinary tract infections, including prosatitis
- Urethritis and cervicitis gonorrhoea
- Gastro-intestinal tract infections, including typhoid fever and paratyphoid
- Respiratory tract infections, except pneumonia caused by streptococcus
- Skin and soft tissue infections
- Bones and joints infections

Consideration should be given to applicable official guidances on the appropriate use of antibacterial agents.

Dosage and method of administration

Unless otherwise prescribed, the following guideline doses are recommended:

● Mild/medium infections of the urinary tract	:	2 X 250 mg/daily
● Severe Infections of the urinary tract	:	2 x 500 mg/daily
● Mild/medium infections of the respiratory tract, bones, joints, skin and soft tissue	:	2 x 500 mg/daily
● Severe infections of the respiratory tract, bones, joints, skin and soft tissue	:	2 x 750 mg/daily
● Infections of the gastro-intestinal tract	:	2 x 500 mg/daily
● Acute gonorrhoea	:	Single dose of 250 mg
● To achieve adequate concentration in acute osteomyelitis, the dosage should not be less than	:	2 x 750 mg/daily

Dosage with impaired renal function

With a creatinine clearance of less than 20 mL/minute, the normal dose (refer to dosage table) must be administered only once daily or reduced by half if taken twice daily.

Method of Administration
The tablet should be swallowed with liquid. They may be taken independently of meals, taking on an empty stomach will accelerate absorption.

Duration of Treatment
The duration of treatment is dependent on severity of the case, as well as on clinical and bacteriological progress.
For acute infections, the treatment normally takes 5 to 10 days.
Generally the treatment should be continued consistently for at least 3 days after defervescence or disappearance of clinical symptoms.

Missed dose
If a dose is missed, it should be taken anytime but not later than 6 hours prior to the next scheduled dose. If less than 6 hours remain before the next dose, the missed dose should not be taken and treatment should be continued as prescribed with the next scheduled dose. Double dose should not be taken to compensate for a missed dose.

Contraindications

Ciproxin should not be used where there is hypersensitivity to ciprofloxacin or to other chemoterapheutic agents of the quinolone group.
Ciproxin should not be prescribed to children, growing adolescents and pregnant or nursing women, as there is no evidence of its safety when used in these groups and, on the basis of results from animal experiments, injury to the articular cartilage of an organism which is not fully grown cannot be completely ruled out.
Animal experiments have not shown any evidence teratogenic effects (malformations).

Special warnings and special precautions for use

- To avoid the incidence of crystalluria, ciproxin tablet should be swallowed with liquid.
- Caution for any intake by patients with impaired renal function (see explanation on dosage)
- Administration should not be more than the dosage indicated

Severe Infections and/or infections due to Gram-positive or anaerobic bacteria
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.

Streptococcus pneumoniae infections
Ciproxin is not recommended for treatment of pneumococcal infections due to limited efficacy against Streptococcus pneumoniae.
Genital tract infections
Epididymo-orchitis and pelvic inflammatory diseases may be caused by fluoroquinolone-resistant *Neisseria gonorrhoeae*. Ciprofloxacin should be co-administered with another appropriate antibacterial agent unless ciprofloxacin-resistant *Neisseria gonorrhoeae* can be excluded. If clinical improvement is not achieved after 3 days of treatment, the therapy should be reconsidered.

Cardiac disorders
Ciproxin is associated with cases of QT prolongation (see '*Undesirable effects*'). As women tend to have a longer baseline QTc interval compared with men, they may be more sensitive to QTc-prolonging medications. Elderly patients may also be more susceptible to drug-associated effects on the QT interval. Precaution should be taken when using Ciproxin with concomitant drugs that can result in prolongation with the QT interval (e.g. class IA or III antiarrhythmics, tricyclic antidepressants, macrolides, antipsychotics) (see '*Interaction with other medicinal products and other forms of interaction*') or in patients with risk factors for QT prolongation or torsade de pointes (e.g. congenital long QT syndrome , uncorrected electrolyte imbalance such as hypokalemia or hypomagnesemia and cardiac disease such as heart failure, myocardial infarction, or bradycardia).

Children and adolescents
As with medicinal products in its class, ciprofloxacin has been shown to cause arthropathy in weight-bearing joints of immature animals. The analysis of available safety data from ciprofloxacin use in patients less than 18 years of age, the majority of whom had cystic fibrosis, did not disclose any evidence of drug-related cartilage or articular damage. The use of Ciproxin for indications other than the treatment of acute pulmonary exacerbation of cystic fibrosis caused by *Pseudomonas aeruginosa* infection (children aged 5 – 17 years), complicated urinary tract infections and pyelonephritis due to *Escherichia coli* (children aged 1 – 17 years), and for the use in inhalational anthrax (post-exposure) was not studied. For other indications clinical experience is limited.

Hypersensitivity
In some instances, hypersensitivity and allergic reactions may occur following a single dose, a physician should be informed immediately.
Anaphylactic/anaphylactoid reactions in very rare instances can progress to a life-threatening shock, in some instances after the first administration. In these cases, ciprofloxacin has to be discontinued and medical treatment (e.g. treatment for shock) is required.

Gastrointestinal System
In the event of severe and persistent diarrhea during or after treatment, a physician must be consulted since this symptom can hide a serious intestinal disease (life-threatening pseudomembranous colitis with possible fatal outcome), requiring immediate treatment. In such cases, Ciproxin must be discontinued and appropriate therapy initiated (e.g. vancomycin, orally, 4 x 250 mg/day). Medicinal products that inhibit peristalsis are contraindicated.

Hepatobiliary system
Cases of hepatic necrosis and life-threatening hepatic failure have been reported with Ciproxin. 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 (see '*Undesirable effects*').
There can be a temporary increase in transaminases, alkaline phosphatase, or cholestatic jaundice, especially in patients with previous liver damage, who are treated with Ciproxin (see '*Undesirable effects*').

Myasthenia Gravis
Ciproxin should be used with caution in patients with myasthenia gravis, because symptoms can be exacerbated.

Tendinitis and tendon rupture
Tendinitis and tendon rupture (predominantly Achilles tendon), sometimes bilateral, may occur with Ciproxin, even within the first 48 hours of treatment. Cases occurring up to several months after completion of therapy have been reported (see '*Undesirable effects*'). The risk of tendinopathy may be increased in elderly patients during strenuous physical activity, in patients treated concomitantly with corticosteroids, in patients with renal impairment and patients with solid organ transplants.

At any sign of tendinitis (e.g. painful swelling, inflammation), the affected extremity should be kept at rest, any inappropriate physical exercise should be avoided, a physician should be consulted and the antibiotic treatment should be discontinued. Ciproxin should be used with caution in patients with a history of tendon disorders related to fluoroquinolone treatment.

Seizures
Ciproxin, like other fluoroquinolones, is known to trigger seizures or lower the seizure threshold. In epileptics and patients who have suffered from previous central nervous system (CNS) disorders (e.g. lowered convulsion threshold, previous history of convulsion, reduced cerebral blood flow, altered brain structure or stroke), Ciproxin should only be used where the benefits of treatment exceed the risks, since these patients are endangered because of possible undesirable CNS effects. Cases of status

epilepticus have been reported (see '*Undesirable effects*'). If seizures occur, Ciproxin should be discontinued.

Psychiatric reactions
Psychiatric reactions may occur even after the first administration of fluoroquinolones, including Ciproxin. In rare cases, depression or psychotic reactions can progress to suicidal ideations/thoughts and self-injurious behavior, such as attempted or completed suicide (see '*Undesirable effects*'). In the event that the patient develops these reactions, Ciproxin should be discontinued and appropriate measures instituted.

Peripheral neuropathy
Cases of sensory or sensorimotor polyneuropathy resulting in paresthesias, hypoesthesias, dysesthesias, or weakness have been reported in patients receiving fluoroquinolones including Ciproxin. Patients under treatment with Ciproxin should be advised to inform their doctor prior to continuing treatment if symptoms of neuropathy such as pain, burning, tingling, numbness, or weakness develop (see '*Undesirable effects*').

Skin and Appendages
Ciprofloxacin has been shown to produce photosensitivity reactions. Patients taking Ciproxin should avoid direct exposure to excessive sunlight or UV-light. Therapy should be discontinued if photosensitization (i.e. sunburn-like skin reactions) occurs.

Cytochrome P450
Ciprofloxacin is known to be a moderate inhibitor of the CYP 450 1A2 enzymes. Care should be taken when other medicinal products which are metabolized via the same enzymatic pathway (e.g., theophylline, methylxantines, caffeine, duloxetine, ropirinole, clozapine, olanzapine, agomelatine) are administered concomitantly. Increased plasma concentrations associated with drug-specific side effects may be observed due to inhibition of their metabolic clearance by ciprofloxacin (see section "Interaction with other medicinal products and other forms of interaction").

Dysglycemia
As with all fluoroquinolones, disturbances in blood glucose, including both hypoglycemia and hyperglycemia have been reported with Ciproxin. In Ciproxin-treated patients, dysglycemia occurred predominantly in elderly diabetic patients receiving concomintant treatment with an oral hypoglycemic agent (e.g. sulfonylurea) or with insulin. In diabetic patients, careful monitoring of blood glucose is recommended (see 'Undesireable effects')

Interaction with tests
Ciprofloxacin in vitro potency may interfere with the *Mycobacterium tuberculosis.* culture test by suppression of mycobacterial growth, causing false negative results in specimens from patients currently taking Ciproxin.

Interaction with other medicaments and other forms of interaction

Drugs known to prolong QT interval
Ciproxin, like other fluoroquinolones, should be used with caution in patients receiving drugs known to prolong the QT interval (e.g. Class IA and III anti-arrhythmics, tricyclic antidepressants, macrolides, antipsychotics) (see '*Special warnings and precautions for use*').

Chelation Complex Formation
The simultaneous administration of Ciproxin (oral) and multivalent cation-containing medicinal products and mineral supplements (e.g. calcium, magnesium, aluminum, iron), polymeric phosphate binders (e.g. sevelamer, lanthanum carbonate), sucralfate or antacids, and highly buffered drugs (e.g. didanosine tablets) containing magnesium, aluminum, or calcium reduce the absorption of ciprofloxacin. Consequently, Ciproxin 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 H_2 receptor blockers.

Food and Dairy Products
The concurrent administration of dairy products or mineral-fortified drinks alone (e.g. milk, yoghurt, calcium-fortified orange juice) and Ciproxin should be avoided because absorption of ciprofloxacin may be reduced. Dietary calcium as part of a meal, however, does not significantly affect absorption.

Probenecid
Probenecid interferes with renal secretion of ciprofloxacin. Co-administration of probenecid containing medicinal products and Ciproxin increases the 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.

Tizanidine
In a clinical study in healthy subjects, there was an increase in tizanidine serum concentrations (C_{max} increase: 7-fold, range: 4 to 21-fold; AUC increase: 10-fold, range: 6 to 24-fold) when given concomitantly with ciprofloxacin. Associated with the increased serum concentrations was a potentiated hypotensive and sedative effect. Tizaninidine containing medicinal products must not be administered together with Ciproxin (*see "Contraindications"*).

Theophylline
Concurrent administration of ciprofloxacin and theophylline containing medicinal products can cause an undesirable increase in the serum theophylline concentration. This can lead to theophylline-induced side effects. In very rare cases, these side effects can be life threatening or fatal. If concurrent use of the two medicinal products is unavoidable, the serum theophylline concentration should therefore be checked and the theophylline dose appropriately reduced (see*"Special warnings and precautions for use"*).

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

Phenytoin
Altered (decreased or increased) serum levels of phenytoin were observed in patients receiving Ciproxin and phenytoin simultaneously. To avoid the loss of seizure control associated with decreased phenytoin levels, and to prevent phenytoin overdose-related undesirable effects when Ciproxin is discontinued in patients receiving both agents, monitoring of phenytoin therapy, including phenytoin serum concentration measurements, is recommended during and shortly after co-administration of Ciproxin with phenytoin.

Methotrexate
Renal tubular transport of methotrexate may be inhibited by concomitant administration of Ciproxin, potentially leading to increased plasma levels of methotrexate. This might increase the risk of methotrexate-associated toxic reactions. Therefore, patients under methotrexate therapy should be carefully monitored when concomitant Ciproxin therapy is indicated.

NSAID
Animal studies have shown that the combination of very high doses of fluoroquinolones (gyrase inhibitors) and certain non-steroidal anti-inflammatory agents (but not acetylsalicylic acid) can provoke convulsions.

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 Ciproxin with a vitamin K antagonist may augment its anticoagulant 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 normalized 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 (see *"Special warnings and precautions for use"*)

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 Cmax and AUC of ropinirole by 60% and 84%, respectively. Monitoring ropinirole-related side effects dose adjustment as appropriate is recommended during and shortly after co-administration with Ciproxin.

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 Ciproxin are advised.

Sildenafil
Cmax 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 Ciproxin 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 (see '*Cytochrome P450*' in section *'Special warnings and precautions for use'*).

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

Pregnancy and lactation
Pregnancy
Since the safety of ciprofloxacin in pregnant women has not been established and since, on the basis of animal studies, it is not entirely improbable that the drug could cause damage to articular cartilage in the immature fetal organism (see Preclinical safety data), ciprofloxacin must not be prescribed to pregnant women.
Animal studies have not shown any evidence of teratogenic effects (malformations).

Lactation
Ciprofloxacin is excreted in breast milk. Due to the potential risk of articular damage, ciprofloxacin should not be used during breast-feeding (see Preclinical safety data).

Effects on ability to drive and use machines

Fluoroquinolones including ciprofloxacin may result in an impairment of the patient's ability to drive or operate machinery due to CNS reactions (see section undesirable effect). This applies particularly in combination with alcohol.

Undesirable effects

Adverse drug reactions (ADRs) based on all clinical studies with ciprofloxacin (oral, parenteral) sorted by CIOMS III categories of frequency are listed below (overall n = 51621).
The frequencies of ADRs reported with ciprofloxacin are summarised in the table below. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to ≤1/100); rare (≥1/10,000 to ≤1/1,000); very rare (≤1/10,000), not known (cannot be estimated from the available data).
The ADRs identified only during postmarketing surveillance, and for which a frequency could not be estimated, are listed under "not known".

System Organ Class	Common	Uncommon	Rare	Very Rare	Not Known
Infections and Infestations		Mycotic superinfections	Antibiotic associated colitis (very rarely with possible fatal outcome)		
Blood and Lymphatic System Disorders		Eosinophilia	Leukopenia Anemia Neutropenia Leukocytosis Thrombocytopenia Thrombocytemia	Hemolytic anemia Agranulocytosis Pancytopenia (life-threatening) Bone marrow depression (life-threatening)	
Immune System Disorders			Allergic reaction Allergic edema / angioedema	Anaphylactic reaction Anaphylactic shock (life-threatening) Serum sickness-like reaction	
Metabolism and Nutrition Disorders		Decreased appetite and food intake	Hyperglycemia Hypoglycemia		

System Organ Class	Common	Uncommon	Rare	Very Rare	Not Known
Psychiatric Disorders		Psychomotor hyperactivity / agitation	Confusion and disorientation Anxiety reaction Abnormal dreams Depression (potentially culminating in self-injurious behavior, such as suicidal ideations / thoughts and attempted or completed suicide) Hallucinations	Psychotic reactions (potentially culminating in self-injurious behavior, such as suicidal ideations / thoughts and attempted or completed suicide)	
Nervous System Disorders		Headache Dizziness Sleep disorders Taste disorders	Par- and Dysesthesia Hypoesthesia Tremor Seizures (including status epilepticus) Vertigo	Migraine Disturbed coordination Smell disorders Hyperesthesia Intracranial hypertension (pseudotumor cerebri)	Peripheral neuropathy and polyneuropathy
Eye Disorders			Visual disturbances	Visual color distortions	
Ear and Labyrinth Disorders			Tinnitus Hearing loss Hearing impaired		
Cardiac Disorders			Tachycardia		QT prolongation, ventricular arrhythmia, torsades de pointes *
Vascular Disorders			Vasodilatation Hypotension Syncope	Vasculitis	
Respiratory, Thoracic and Mediastinal Disorders			Dyspnea (including asthmatic condition)		
Gastrointestinal Disorders	Nausea Diarrhea	Vomiting Gastrointestinal and abdominal pains Dyspepsia Flatulence		Pancreatitis	
Hepatobiliary Disorders		Increase in transaminases Increased bilirubin	Hepatic impairment Jaundice Hepatitis (non infective)	Liver necrosis (very rarely progressing to life-threatening hepatic failure)	

System Organ Class	Common	Uncommon	Rare	Very Rare	Not Known
Skin and Subcutaneous Tissue Disorders		Rash Pruritus Urticaria	Photosensitivity reactions Blistering	Petechiae Erythema multiforme Erythema nodosum Stevens-Johnson syndrome (potentially life-threatening) Toxic epidermal necrolysis (potentially life-threatening)	Acute generalized exanthematous pustulosis (AGEP)
Musculoskeletal, Connective Tissue and Bone Disorders		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 Hematuria Crystalluria Tubulointerstitial nephritis		
General Disorders and Administration Site Conditions		Unspecific pain Feeling unwell Fever	Edema Sweating (hyperhidrosis)	*Gait disturbance*	
Investigations		Increase in blood alkaline phosphatase	Abnormal prothrombin level, Increased amylase		International normalized ratio (INR) increased (in patients treated with Vitamin K antagonists)

*These events were reported during the postmarketing period and were observed predominantly among patients with further risk factors for QT prolongation (see section special warnings and precautions for use).

In isolated instances, some serious adverse drug reactions may be long-lasting (> 30 days) and disabling; such as tendinitis, tendon rupture, musculoskeletal disorders, and other reactions affecting the nervous system including psychiatric disorders and disturbance of senses.

The following undesirable effects have a higher frequency category in the subgroups of patients receiving intravenous or sequential (intravenous to oral) treatment:

Common	Vomiting, Transient increase in transaminases, Rash
Uncommon	Thrombocytopenia, Thrombocytaemia, Confusion and disorientation, Hallucinations, Par- and dysaesthesia, Seizures, Vertigo, Visual disturbances, Hearing loss, Tachycardia, Vasodilatation, Hypotension, Transient hepatic impairment, Jaundice, Renal failure, Oedema
Rare	Pancytopenia, Bone marrow depression, Anaphylactic shock, Psychotic reactions, Migraine, Smell disorders, Hearing impaired, Vasculitis, Pancreatitis, Liver necrosis, Petechiae, Tendon rupture

Overdose

In the event of acute, excessive oral overdosage, reversible renal toxicity has been reported in some cases.
Apart from routine emergency measures, 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 reduce the absorption of ciprofloxacin in overdoses.
Only a small quantity of ciprofloxacin (< 10%) is eliminated by hemodialysis or peritoneal dialysis.

Presentation

CIPROXIN® 500 mg Box, 2 blisters @ 10 film-coated tablets

Instruction for use/handling :

Storage
Store below 30 °C
Keep drugs out of reach of children

Harus dengan resep dokter

Ciproxin® 500 mg: Reg. No. XXXXXXXXXXXXXX

Made by Bayer AG, Leverkusen Germany
Imported and packed by PT. Bayer Indonesia, Depok - Indonesia