SUMMARY OF PRODUCTS CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Q-BACT 500 TABLETS
Ciprofloxacin Tablets USP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:
Ciprofloxacin Hydrochloride USP

Equivalent to Ciprofloxacin	:	500 mg
Excipients	:	Q.S.
Colour	:	Quinoline Yellow

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Tablet
For oral administration

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Q-BACT 500 TABLETS are indicated for the treatment of the following infections.

Adults

- Lower respiratory tract infections due to Gram-negative bacteria
  - Broncho-pulmonary infections in cystic fibrosis or in bronchiectasis
  - Pneumonia
- Acute exacerbation of chronic bronchitis and of chronic obstructive pulmonary disease
  - Acute exacerbation of chronic obstructive pulmonary disease including chronic bronchitis
  - Acute exacerbations of chronic bronchitis
  - Exacerbation of chronic obstructive pulmonary disease
- Otitis media acute
- Acute bacterial rhinosinusitis
  - Acute sinusitis
  - Acute bacterial sinusitis
- Urinary tract infections
  - Uncomplicated acute cystitis
    - Simple uncomplicated acute cystitis
    - Acute cystitis in women
    - Simple uncomplicated acute cystitis in the premenopausal adult women
    - Recurrent cystitis in women
    - Acute uncomplicated infection of lower urinary tract (simple cystitis)
    - Acute pyelonephritis
    - Complicated urinary tract infections
    - Bacterial prostatitis
- Gonococcal uretritis and cervicitis

- Epididymo-orchitis including cases due to Neisseria gonorrhoeae
- Pelvic inflammatory disease including cases due to Neisseria gonorrhoeae
- In the above genital tract infections when thought or known to be due to Neisseria gonorrhoeae it is particularly important to obtain local information on the prevalence of resistance to ciprofloxacin and to confirm susceptibility based on laboratory testing.
- Intra-abdominal infections
- Infections of the skin and soft tissue caused by Gram-negative bacteria
- Infections of the bones and joints
- Ciprofloxacin may be used in the management of neutropenic patients with fever that is suspected to be due to a bacterial infection
- Prophylaxis of invasive infections due to Neisseria meningitidis
- Inhalation anthrax (post-exposure prophylaxis and curative treatment)

Paediatric population and adolescents
- Broncho-pulmonary infections due to Pseudomonas aeruginosa in patients with cystic fibrosis
- Complicated urinary tract infections and acute pyelonephritis
- Inhalation anthrax (post-exposure prophylaxis and curative treatment)

4.2 Posology and method of administration

Adults

<table>
<tr><th colspan="2">Indications</th><th>Daily dose inmg</th><th>Total duration oftreatment (potentially including initial parenteral treatment with ciprofloxacin)</th></tr>
<tr><td colspan="2">Infections of the lower respiratorytract</td><td>500 mg twice daily to
750 mg twice daily</td><td>7 to 14 days</td></tr>
<tr><td rowspan="2">Acute exacerbationof chronic bronchitis and of chronic obstructive pulmonary disease</td><td>Acute exacerbationof chronic obstructive pulmonary diseaseincluding chronic bronchitis</td><td>500 mg twice daily to
750 mg twice daily</td><td>7 to 14 days</td></tr>
<tr><td>Acute exacerbationsof chronic bronchitis</td><td>500 mg twice daily to
750 mg twice daily</td><td>7 to 14 days</td></tr>
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	Exacerbation of chronic obstructive pulmonary disease	500 mg twice daily to 750 mg twice daily	7 to 14 days
Otitis media acute		500 mg twice daily to 750 mg twice daily	7 to 14 days
Acute bacterial rhinosinusitis		500 mg twice daily to 750 mg twice daily	7 to 14 days
Urinary tractinfections	Uncomplicat edacute cystitis	250 mg twice daily to 500 mg twice daily	3 days
		In pre-menopausal women, 500 mg single dose may be used	
	Acute pyelonephritis	500 mg twice daily	7 days
	Complicated urinarytract infections	500 mg twice daily to 750 mg twice daily	at least 10 days, itcan be continued for longer than 21 days in some specific circumstances (such as abscesses)
	Bacterial Prostatitis	500 mg twice	2 to 4 weeks

Paediatric population and adolescents

Indications	**Daily dose in mg**	**Total duration of treatment (potentially including initial parenteral treatment with ciprofloxacin)**
Broncho-pulmonary	20 mg/kg body weight twice daily with a maximum of	10 to 14 days
infections due to *Pseudomonasaeruginosa* in patients with cystic fibrosis	750 mg per dose.	
Complicated urinary tract infections and acute 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 whenclinically appropriate). Drug administration should begin as soon as possibleafter 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
Geriatric patients should receive a dose selected according to the severity ofthe 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 m²]	**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

Method of Administration
Oral
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.

4.3 Contraindications

- Hypersensitive to the active substance or to any of the excipients listed in section 6.1.
- 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 coadministered 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 be co-administered 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.

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 and adolescents

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.

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 acute 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 (see section 4.8) 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

Tendinitis and tendon rupture (especially but not limited to Achilles tendon), sometimes bilateral, may occur as early as within 48 hours of starting treatment with quinolones and fluoroquinolones and have been reported to occur even up to several months after discontinuation of treatment. The risk of tendinitis and tendon rupture is increased in older patients, patients with renal impairment, patients with solid organ transplants, and those treated concurrently with corticosteroids. Therefore, concomitant use of corticosteroids should be avoided.

At the first sign of tendinitis (e.g. painful swelling, inflammation) the treatment with Ciprofloxacin should be discontinued and alternative treatment should be considered. The affected limb(s) should be appropriately treated (e.g. immobilisation).

Corticosteroids should not be used if signs of tendinopathy occur.

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

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 (see section 4.8).

Psychiatric reactions may occur even after the first administration of ciprofloxacin. In rare cases, depression or psychosis can progress to endangering behaviour and suicidal ideations/thoughts culminating in attempted suicide or completed suicide. In these cases, ciprofloxacin should be discontinued.

Peripheral neuropathy

Cases of sensory or sensorimotor polyneuropathy resulting in paraesthesia, hypaesthesia, dysesthesia, or weakness have been reported in patients receiving quinolones and fluoroquinolones. Patients under treatment with Ciprofloxacin should be advised to inform their doctor prior to continuing treatment if symptoms of neuropathy such as pain, burning, tingling, numbness, or weakness develop in order to prevent the development of potentially 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 recommended.

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 (see section 4.8). 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 described in section 4.2 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 (see section 4.8). 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.

Vision disorders

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

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). Co-administration of ciprofloxacin and tizanidine is contra-indicated. 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.
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.

Epidemiologic studies report an increased risk of aortic aneurysm and dissection after intake of fluoroquinolones, particularly in the older population.

Therefore, fluoroquinolones should only be used after careful benefit-risk assessment and after consideration of other therapeutic options in patients with positive family history of aneurysm disease, or in patients diagnosed with pre-existing aortic aneurysm and/or aortic dissection, or in presence of other risk factors or conditions predisposing for aortic aneurysm and dissection (e.g. Marfan syndrome, vascular Ehlers-Danlos syndrome, Takayasu arteritis, giant cell arteritis, Behcet's disease, hypertension, known atherosclerosis).
In case of sudden abdominal, chest or back pain, patients should be advised to immediately consult a physician in an emergency department.
Prolonged, disabling and potentially irreversible serious adverse drug reactions
Very rare cases of prolonged (continuing months or years), disabling and potentially irreversible serious adverse drug reactions affecting different, sometimes multiple, body systems (musculoskeletal, nervous, psychiatric and senses) have been reported in patients receiving quinolones and fluoroquinolones irrespective of their age and pre-existing risk factors. Ciprofloxacin should be discontinued immediately at the first signs or symptoms of any serious adverse reaction and patients should be advised to contact their prescriber for advice.

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 the 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 Cmax and AUC of ciprofloxacin.

Effects of ciprofloxacin on other medicinal products:

Tizanidine

Tizanidine must not be administered together with ciprofloxacin (see section 4.3). In a clinical study with healthy subjects, there was an increase in serum tizanidine concentration (Cmax 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. There have been many reports of increases in oral anticoagulant activity in patients receiving antibacterial agents, including fluoroquinolones. 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 Cmax 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 Cmax 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

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 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 ciprofloxacin may increase blood levels of zolpidem, concurrent use is not recommended.

4.6 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 Ciprofloxacin (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 available data)
Infections and Infestations		Mycotic superinfections	Antibiotic associated colitis (very rarely with possible fatal outcome) (see section 4.4)		
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) (see section 4.4), Serum sickness like reaction	
Metabolism and Nutrition Disorders		Decreased appetite, Anorexia	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, Hypomania
Nervous System Disorders*		Headache, Dizziness, Sleep, disorders, Taste disorders	Par- and Dysaesthesia, Hypoaesthesia, Tremor, Seizures (incl. status epilepticus see section 4.4), Vertigo	Migraine, Disturbed Coordination, Gait Disturbance, Olfactory nerve Disorders, Intracranial Hypertensi	Peripheral Neuropathy and polyneuropathy

				on and pseudotum or cerebri	
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 (see section 4.4 and 4.9)
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		Pancreatitis	

Hepatobiliary Disorders		Increase in Transaminases, Increased bilirubin	Hepatic Impairment, Cholestatic icterus, Hepatitis	Liver necrosis (very rarely progressing to life-threatening hepatic failure) (see section	
Skin and Subcutaneous Tissue Disorders		Rash, Pruritus, Urticaria	Photosensitivity reactions (see section 4.4)	Petechiae, Erythema Multiforme, Erythema Nodosum, Stevens-Johnson syndrome (potentially lifethreatening), Toxic epidermal necrolysis (potentially lifethreatening)	Acute generalised exanthematous pustulosis (AGEP), DRESS
Musculoskeletal, Connective Tissue and Bone 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) (see section 4.4), Exacerbation of symptoms of	

				myasthenia gravis (see section 4.4)	
Renal and Urinary Disorders		Renal impairment	Renal failure, Haematuria, Crystalluria (see section 4.4), Tubulointerstitial nephritis		
General Disorders and Administration Site Conditions*		Asthenia, Fever	Oedema, Sweating (hyperhidrosis)		
Investigations		Increase in blood alkaline phosphatase	Prothrombin level Abnormal, Increased amylase		International normalised ratio increased (in patients treated with Vitamin K antagonists)

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.
In the event of overdose, symptomatic treatment should be implemented. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation.
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.

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.

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 (Cmax) 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 nonionised 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 (M1-M4)	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.

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Name of Material	Specification
Maize Starch	BP
Microcrystalline Cellulose	BP
Croscarmellose Sodium	BP
Polysorbate 80	BP
Purified water	BP
Magnesium stearate	BP
Purified Talc	BP
Film Coating Quinoline Yellow	IHS
Isopropyl Alcohol	BP

6.2 Incompatibilities
NA

6.3 Shelf life
36 Months

6.4 Special precautions for storage
Store below 30°C. Protected from light.
KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container
10 x 10 Tablets in Alu-PVC pack is packed in a printed carton along with a package insert.

6.6 Instructions for use and handling
No special requirements.

7. MARKETING AUTHORISATION HOLDER

Ahmedabad
Gujarat, India.
E-mail: info@sagalabs.com
URL: www.sagalabs.com

8. NUMBER(S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS

06875/08816/NMR/2021

9. DATE OF FIRSHT AUTHORISATION/RENEWAL OF THE AUTHORISATION

28/11/2021

10. DATE OF REVISION OF THE TEXT

01 April 2026