Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ciprofloxacin 2 mg/ml Solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of solution for infusion contains 2 mg of ciprofloxacin.

Excipient(s)with known effect:
Contains 30.8 mmol (707.70 mg) sodium per 200 ml of solution for infusion, equivalent to 35.39 % of the WHO recommended daily intake for sodium for an adult.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion.

Clear, yellowish, sterile and non-pyrogenic aqueous solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Ciprofloxacin 2 mg/ml Solution for infusion is indicated for the treatment of the following infections (see sections 4.4 and 5.1). Special attention should be paid to available information on resistance to ciprofloxacin before commencing therapy.

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

Adults

- Lower respiratory tract infections due to Gram-negative bacteria

- exacerbations of chronic obstructive pulmonary disease (COPD). For exacerbation of COPD, Ciprofloxacin 2 mg/ml Solution for infusion should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.
- 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

- acute pyelonephritis
- complicated urinary tract infections
- bacterial prostatitis

- Genital tract infections -epididymo-orchitis including cases due to susceptible *Neisseria gonorrhoeae* -pelvic inflammatory disease (PID) 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
- Inhalation of anthrax pathogens (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.

Paediatric population

- Broncho-pulmonary infections due to *Pseudomonas aeruginosa* in patients with cystic fibrosis
- Complicated urinary tract infections and acute pyelonephritis
- Inhalation of anthrax pathogens (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 a physician experienced in the treatment of cystic fibrosis and/or severe infections in children and adolescents (see sections 4.4 and 5.1).

4.2 Posology and method of administration

Posology
The dosage is determined by the indication, severity and site of infection, susceptibility to ciprofloxacin of the causative organism(s), the renal function of the patient and, in children and adolescents body weight.

The duration of treatment depends on the severity of the illness and on the clinical and bacteriological course.

After intravenous initiation of treatment, the treatment can be switched to treatment with tablets or suspension if clinically indicated, at the discretion of the treating physician. Such a switch from the intravenous to the oral form of administration should be made as soon as possible.
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 dosing is possible.

Treatment of infections due to certain pathogens (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 (PID), intra-abdominal infections, infections in neutropenic patients and infections of bones and joints) may require additional administration of other antibacterial agents depending on the pathogens involved.

Adults

Therapeutic indications		**Daily dose in mg**	**Total duration of treatment (including switch to oral therapy as soon as possible)**
Infections of the lower respiratory tract		400 mg twice daily to 400 mg three times daily	7 to 14 days
Infections of the upper respiratory tract	Acute exacerbation of chronic sinusitis	400 mg twice daily to 400 mg three times daily	7 to 14 days
	Chronic suppurative otitis media	400 mg twice daily to 400 mg three times daily	7 to 14 days
	Malignant external otitis	400 mg three times daily	28 days up to 3 months
Urinary tract infections (see section 4.4)	Complicated urinary infections and	400 mg twice daily to 400 mg three times daily	7 to 21 days, it can be continued for longer than 21 days in some specific circumstances (such as abscesses)

	acute pyelonephritis		
	Bacterial prostatitis	400 mg twice daily to 400 mg three times daily	2 to 4 weeks (acute)
Genital tract infections	Epididymo-orchitis and pelvic inflammatory diseases, including cases caused by susceptible *Neisseria gonorrhoeae*	400 mg twice daily to 400 mg three times daily	at least 14 days
Infections of the gastro-intestinal tract and intraabdominal infections	Diarrhoea caused by bacterial pathogens including *Shigella spp. other than Shigella dysenteriae* type 1 and empirical treatment of severe travellers' diarrhoea	400 mg twice daily	1 day
	Diarrhoea caused by *Shigella dysenteriae type 1*	400 mg twice daily	5 days
	Diarrhoea caused by *Vibrio cholerae*	400 mg twice daily	3 days
	Typhoid fever	400 mg twice daily	7 days
	Intra-abdominal infections due to Gram-negative bacteria	400 mg twice daily to 400 mg three times daily	5 to 14 days
Infections of the skin and soft tissue, caused by Gram-negative bacteria		400 mg twice daily to 400 mg three times daily	7 to 14 days
Infections of the bones and joints		400 mg twice daily to 400 mg three times daily	3 months maximum
Neutropenic patients with fever that is suspected to be due to a bacterial infection. Ciprofloxacin should be		400 mg twice daily to 400 mg three times daily	Therapy should be continued over the entire period of neutropenia

combined with appropriate antibacterial agents in accordance with official recommendations.			
Inhalation of anthrax pathogens post-exposure prophylaxis and curative treatment for persons requiring parenteral treatment Treatments should be started as soon as possible after suspected or confirmed exposure.		400 mg twice daily	60 days from confirmation of *Bacillus anthracis* exposure

Paediatric population

Therapeutic indications	**Daily dose in mg**	**Total duration of treatment (including switch to oral therapy as soon as possible)**
Cystic fibrosis	10 mg/kg body weight three times daily with a maximum single dose of 400 mg	10 to 14 days
Complicated urinary tract infections and acute pyelonephritis	6 mg/kg body weight three times daily to 10 mg/kg body weight three times daily with a maximum single dose of 400 mg	10 to 21 days
Inhalation of anthrax	10 mg/kg body	60 days from the confirmation of *Bacillus anthracis* exposure

pathogens post-exposure curative treatment for persons requiring parenteral treatment Treatment should be started as soon as possible after suspected or confirmed exposure	weight twice daily to 15 mg/kg body weight twice daily with a maximum single dose of 400 mg	
Other severe infections	10 mg/kg body weight three times daily with a maximum daily dose of 400 mg	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 impaired renal and/or hepatic function
Recommended starting and maintenance doses for patients with impaired renal function:

Creatinine clearance [mL/min/1.73 m^2]	**Serum creatinine [micromole/L]**	**Intravenous dose [mg]**
> 60	< 124	See usual dosage
30-60	124 to 168	200-400 mg every 12 h
< 30	> 169	200-400 mg every 24 h
Patients on haemodialysis	> 169	200-400 mg every 24 h (after dialysis)
Patients on peritoneal dialysis	> 169	200-400 mg every 24 h

For patients with impaired hepatic function no dose adjustment is required.
The dosage for children with impaired renal and/or hepatic function has not been studied.

Method of administration
Ciprofloxacin 2 mg/ml Solution for infusion must be inspected visually prior to use. It must not be used if cloudy.

Ciprofloxacin should be administered by intravenous infusion. For children, the infusion duration is 60 minutes.

In adults, the infusion time is 60 minutes for 400 mg Ciprofloxacin 2 mg/ml Solution for infusion. and 30 minutes for 200 mg Ciprofloxacin 2 mg/ml Solution for infusion. Slow infusion into a large vein will minimise patient discomfort and reduce the risk of venous irritation.

The solution for infusion can be infused either directly or after mixing with other compatible solutions for infusion (see section 6.6).

4.3 Contraindications

- Hypersensitivity to the active substance, other quinolones or to any of the excipients listed in section 6.1.

- Concomitant administration of ciprofloxacin and tizanidine (see section 4.5).

4.4 Special warnings and precautions for use

The use of ciprofloxacin should be avoided in patients who have experienced serious adverse reactions in the past when using medicinal products containing quinolone or fluoroquinolone (see section 4.8). Treatment of these patients with ciprofloxacin should only be initiated in the absence of alternative treatment options and after careful benefit/risk assessment (see also section 4.3).

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
Epididymo-orchitis and pelvic inflammatory diseases may be caused by fluoroquinolone-resistant *Neisseria gonorrhoeae* strains.

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 recommended to take into account the local prevalence of resistance in *Escherichia coli* to fluoroquinolones.

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.

Inhalation of anthrax pathogens
Recommended use in humans is based mainly on in-vitro susceptibility testing data and on animal experimental data together with limited human data. Treatment should proceed in consideration of the relevant national and /or international guidelines.

Paediatric population
Official recommendations should be taken into account when administering ciprofloxacin in children and adolescents. 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.

In animal studies. ciprofloxacin has been shown to cause arthropathy in weight-bearing joints of juvenile animals. Safety data from a randomised double-blind study on ciprofloxacin administration to children (ciprofloxacin: n = 335, mean age = 6.3 years; control group: n = 349, mean age = 6.2 years; age range = 1 to 17 years) revealed an incidence of suspected drug-induced arthropathy (based on joint-related clinical findings) occurred in 7.2% and 4.6% by Day +42. The 1-year follow-up revealed an incidence of drug-induced arthropathy of 9.0% and 5.7%. The increased frequency of suspected cases of arthropathy over time was not statistically significant between the two groups. Due to possible adverse reactions on joints and/or surrounding tissue, ciprofloxacin should only be used after careful benefit/risk assessment (see section 4.8).

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 recommendations, 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 anaphylactic and anaphylactoid reactions, may occur following a single dose (see section 4.8) and may be life-threatening. In such cases, ciprofloxacin must be discontinued and an adequate medical treatment is required.

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 have been reported in patients receiving quinolones and fluoroquinolones, affecting different, sometimes multiple, body systems (musculoskeletal, nervous, psychiatric and senses), 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 (see section 4.8).

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.

Ciprofloxacin should be used with caution in patients with myasthenia gravis, because symptoms can be exacerbated (see section 4.8).

Tendinitis and tendon rupture

Ciprofloxacin should generally not be used in patients with a positive history of tendon disease/disorder occurring in association with quinolone treatment. Nevertheless, in very rare cases, after microbiological documentation of the pathogen and careful benefit/risk assessment, ciprofloxacin may be prescribed to these patients for the treatment of certain severe infections, particularly after failure of standard therapy or in the presence of bacterial resistance, where the microbiological data justify the use of ciprofloxacin.

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 in patients treated concurrently with corticosteroids. Therefore, concomitant use of corticosteroids should be avoided.

At the first sign of tendinitis (e.g. painful swelling, inflammation), treatment with ciprofloxacin should be discontinued and alternative treatment should be considered. The affected limbs should be appropriately treated (e.g. immobilisation). Corticosteroids should not be used if signs of tendinopathy occur.

Patients with myasthenia gravis

Ciprofloxacin should be used with caution in patients with myasthenia gravis, as symptoms may be aggravated (see section 4.8).

Aortic aneurysm and dissection, and heart valve regurgitation/incompetence

Epidemiologic studies report an increased risk of aortic aneurysm and dissection, particularly in elderly patients, and of aortic and mitral valve regurgitation after use of fluoroquinolones. Cases of aortic aneurysm and dissection, sometimes complicated by rupture (including fatal cases), as well as regurgitation/incompetence of any of the heart valves have been reported in patients receiving fluoroquinolones (see section 4.8).

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 congenital heart valve defects, or in patients with a diagnosed aortic aneurysm and/or diagnosed aortic dissection or a diagnosed heart valve defect, or in presence of other risk factors or conditions predisposing

- for both aortic aneurysm and dissection and heart valve regurgitation/incompetence (e.g. connective tissue disorders such as Marfan's syndrome or Ehlers-Danlos syndrome, Turner's syndrome, Behcet's disease, hypertension, rheumatoid arthritis) or additionally
- for aortic aneurysm and dissection (e.g. vascular disorders such as Takayasu's arteritis or giant cell arteritis, or known atherosclerosis, or Sjögren's syndrome), or additionally
- for heart valve regurgitation/incompetence (e.g. infective endocarditis).
The risk of aortic aneurysm and dissection, and their rupture may also be increased in patients treated concurrently with systemic corticosteroids.
In case of sudden abdominal, chest or back pain, patients should be advised to immediately consult a physician in an emergency department.
Patients should be advised to seek immediate medical attention in case of dyspnoea, new onset of heart palpitations, or development of oedema in the abdomen or lower extremities.

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 (see section 4.8).

Seizures
Ciprofloxacin like other quinolones are known to potentially trigger seizures or lower the seizure threshold. Cases of status epilepticus have been reported. Hence, ciprofloxacin should be used with caution in patients with disorders of the central nervous system that predispose to seizures. If seizures occur, ciprofloxacin must be discontinued immediately (see section 4.8).

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 damage (see section 4.8).

Psychiatric reactions
Psychiatric reactions may occur even after first administration of ciprofloxacin. In rare cases, depression or psychosis may be accompanied by suicidal thoughts/ideation that may culminate in attempted suicide or completed suicide. If depression, psychotic reactions, suicidal thoughts or behaviour occur, ciprofloxacin must be discontinued immediately.

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 medicinal products 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 disorders (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.
(see section 4.2 Elderly patients, section 4.5, section 4.8, section 4.9).

Dysglycaemia
As with all quinolones, disturbances in blood glucose values, including hypoglycaemia and hyperglycaemia have been reported (see section 4.8), usually in elderly people with diabetes receiving concomitant treatment with an oral antidiabetic agent (e.g., glibenclamide) or with insulin. Cases of hypoglycaemic coma have been reported. In diabetic patients, careful monitoring of blood glucose values is recommended.

Gastrointestinal tract
The occurrence of severe and persistent diarrhoea during or after treatment (including several weeks after treatment) may indicate an antibiotic-associated colitis (possibly life-threatening with fatal outcome), requiring immediate treatment (see

section 4.8). In such cases, ciprofloxacin must be discontinued immediately and appropriate therapy initiated. Antiperistaltic agents 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). At the onset of any signs and symptoms of hepatic disease (such as anorexia, jaundice, dark urine, pruritus, or abdominal tenderness), treatment should be discontinued.

Glucose-6-phosphate dehydrogenase deficiency
Haemolytic reactions have been reported during treatment 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 after 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 lead to increased serum concentration of concomitantly administered substances metabolised via this system (e.g. theophylline, clozapine, olanzapine, ropinirole, tizanidine, duloxetine, agomelatine). Therefore, patients taking these substances concomitantly with ciprofloxacin should be monitored closely for signs of overdose, and determination of serum concentrations (e.g. theophylline) may be necessary (see section 4.5). Combined use of ciprofloxacin and tizanidine is contraindicated.

Methotrexate
Concomitant use of ciprofloxacin and methotrexate is not recommended (see section 4.5).

Interaction with laboratory tests
The *in-vitro* activity of ciprofloxacin against *Mycobacterium tuberculosis* might give false negative bacteriological test results in specimens from patients currently taking ciprofloxacin.

Injection site reactions
Local intravenous site reactions have been reported with the intravenous administration of ciprofloxacin. These reactions are more frequent if the infusion time is 30 minutes or less. These may appear as local skin reactions which resolve rapidly upon completion of the infusion. Subsequent intravenous administration is not contraindicated unless the reactions recur or worsen.

Information on excipients

Sodium
This medicinal product contains 707.70 mg sodium per 200 ml, equivalent to 35.39% of the WHO recommended maximum daily intake for sodium.
The maximum daily dose of this product is equivalent to 106.2 % of the WHO recommended maximum daily intake for sodium.
Appropriate consideration should be taken when administering this product to children.
Ciprofloxacin is considered high in sodium. This should be particularly taken into account for those on a low sodium diet, e.g. patients for whom sodium uptake represents a medical problem (patients with congestive heart failure, heart failure, nephrotic syndrome, etc.).

4.5 Interaction with other medicinal products and other forms of interaction

Effects of other medicinal products on ciprofloxacin:

Medicinal products known to prolong QT interval

Ciprofloxacin, like other fluoroquinolones, should be used with caution in patients receiving medicinal products known to prolong QT interval (e.g. class IA and III anti-arrhythmics, tricyclic antidepressants, macrolides, antipsychotics) (see section 4.4).

Probenecid

Probenecid interferes with renal secretion of ciprofloxacin. Co-administration of probenecid and ciprofloxacin increases ciprofloxacin serum concentrations.

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 (see section 4.4).

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 (see section 4.4).

Other xanthine derivatives

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

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.

Ciyclosporin

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

Concomitant administration of ciprofloxacin and 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 isoenzyme 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 section 4.4).

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 (see section 4.4).

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
Concomitant use of 250 mg ciprofloxacin and 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 (see section 4.4).

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
Clinical studies showed that fluvoxamine, a potent inhibitor of the CYP450 1A2 isoenzyme, significantly inhibits the metabolism of agomelatine. This leads to a 60-fold increase in agomelatine exposure. There are no clinical data regarding the interaction with ciprofloxacin, a moderate inhibitor of the CYP450 1A2 isoenzyme. However, similar effects are expected with concomitant use (see section 4.4).

Zolpidem
Concomitant use of ciprofloxacin and zolpidem may lead to increased zolpidem blood levels. Concomitant use is therefore not recommended.

4.6 Fertility, pregnancy and lactation

Pregnancy
Available data on the use of ciprofloxacin in pregnant women indicate 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, effects on immature cartilage have been observed upon quinolone exposure. Hence, it cannot be excluded that the active substance causes damage to articular cartilage in the infant or juvenile organism / foetus (see section 5.3).
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 and use machines may be impaired.

4.8 Undesirable effects

The most commonly reported adverse drug reactions (ADRs) are nausea, diarrhoea, vomiting, transient increase in transaminases, skin rash, and injection and infusion site reactions.

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 OrganClass	**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		Superinfection fungal			
Blood and lymphatic		Eosinophilia	Leukocytopenia Anaemia	Haemolytic anaemia	

system disorders			Neutropenia Leukocytosis Thrombocythemia	Agranulocytosis Pancytopenia (life-threatening) Bone marrow depression (life-threatening)	
Immune system disorders			Allergic reaction Allergic oedema / angioedema	Anaphylactic reaction Anaphylactic shock (life-threatening) (see section 4.4) Serum sickness-like reaction	
Metabolism and nutrition disorders		Decreased appetite	Hyperglycaemia Hypoglycaemia (see section 4.4)		Hypoglycaemic coma (see section 4.4)
Endocrine disorders					Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
Psychiatric disorders*		Psychomotor hyperactivity / agitation	Confusion and disorientation Anxiety state Nightmares Depression (potentially culminating in suicidal ideations/thoughts or suicide attempts and completed suicide) (see section 4.4) Hallucinations	Psychotic reactions (potentially culminating in suicidal ideations/ thoughts or suicide attempts and completed suicide) (see section 4.4)	Mania, including hypomania
Nervous system disorders*		Headache Drowsiness Sleep disorders Taste disorders	Par- and dysaesthesia Hypoaesthesia Tremor Seizures (including status epilepticus see section 4.4) Lightheadedness	Migraine Coordination disturbance Gait disturbance Olfactory nerve disorders Intracranial hypertension and pseudotumor cerebri	Peripheral neuropathy and polyneuropathy (see section 4.4)
Eye disorders*			Vision disorders (e.g. diplopia)	Visual colour distortions	
Ear and labyrinth			Tinnitus Hearing loss /		

disorders*			Hearing impaired		
Cardiac disorders**			Tachycardia		Ventricular arrhythmia, torsades de pointes (reported predominantly in patients with risk factors for QT prolongation), Electrocardiogram QT interval prolonged (see sections 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 pain Dyspepsia Distention	Antibiotic-associated colitis (very rarely with possible fatal outcome) (see section 4.4)	Pancreatitis	
Hepatobiliary disorders		Increase in transaminases Increased bilirubin	Hepatic impairment Cholestatic icterus Hepatitis	Hepatic necrosis (very rarely progressing to life-threatening hepatic failure) (see section 4.4)	
Skin and subcutaneous tissue disorders		Rash Pruritus Urticaria	Photosensitivity reactions (see section 4.4)	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. pain in extremities, back pain, chest pain) Arthralgia	Myalgia Arthritis Increased muscle tone and cramping	Myasthenia 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 dysfunciton	Renal failure Haematuria Crystalluria (see section 4.4) Tubulointerstitial nephritis		
General disorders and administration site conditions*	Injection and infusion site reactions (only intravenous administration)	Asthenia Fever	Oedema Sweating (hyperhidrosis)		
Investigations		Increase in blood alkaline phosphatase	Increased amylase		International normalised ratio increased (in patients treated with Vitamin K antagonists)

*Very rare cases of prolonged (up to months or years), disabling and potentially irreversible serious drug reactions affecting several, sometimes multiple, system organ classes and senses (including reactions such as tendonitis, tendon rupture, arthralgia, pain in extremities, gait disturbance, neuropathies associated with paraesthesia and neuralgia, fatigue, psychiatric symptoms (including sleep disorders, anxiety, panic attacks, depression and suicidal ideation), memory and concentration impairment, and impairment of hearing, vision, taste and smell) have been reported in association with the use of quinolones and fluoroquinolones in some cases irrespective of pre-existing risk factors (see Section 4.4).
** Cases of aortic aneurysm and dissection, sometimes complicated by rupture (including fatal ones), and of regurgitation/incompetence of any of the heart valves have been reported in patients receiving fluoroquinolones (see section 4.4).

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, skin rash
Uncommon	Thrombocytopenia, thrombocythemia, confusion and disorientation, hallucinations, par- and dysaesthesia, seizures, lightheadedness, visual disorders, hearing loss, tachycardia, vasodilatation, hypotension, transient hepatic impairment, Cholestatic icterus, renal failure, oedema
Rare	Pancytopenia, bone marrow depression, anaphylactic shock, psychotic reaction, migraine, olfactory nerve disorders, hearing impaired, vasculitis, pancreatitis, hepatic necrosis, petechiae, tendon rupture

Paediatric population

The above-mentioned incidence of arthropathy (arthralgia, arthritis), refers to data collected in studies with adults. It has been reported that arthropathy in children is common (see section 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRAPharmacovigilance, Website: www.hpra.ie.

4.9 Overdose

An overdose of 12g 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 of an overdose are: drowsiness, tremor, headache, tiredness, seizures, hallucinations, confusion, abdominal discomfort, impaired renal and hepatic function as well as crystalluria and haematuria. Reversible renal toxicity has been reported.

Apart from routine emergency measures, e.g. gatsric emptying and subsequent administration of activated charcoal, it is recommended that renal function is monitored, including determination of urinary pH, with acidification, if required, to prevent

crystalluria. Adequate hydration must be ensured. Antacids containing calcium or magnesium may theoretically reduce the absorption of ciprofloxacin in case of overdose.

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 antibiotic, 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 bacterial pathogens and the relation between the area under the curve (AUC) and the minimum inhibitory concentration.

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.

Susceptibility testing breakpoints
MIC (minimum inhibitory concentration) interpretive criteria for susceptibility testing have been established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for ciprofloxacin and are listed here:
https://www.ema.europa.eu/documents/other/minimum-inhibitory-concentration-mic-breakpoints_en.xlsx"

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. Expert advice should be sought when the local prevalence of resistance is such that the use of the agent in at least some types of infections is questionable.

Groupings of relevant pathogens according to ciprofloxacin susceptibility (for *Streptococcus* species see section 4.4)

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 acne

INHERENTLY RESISTANT ORGANISMS

Aerobic Gram-positive micro-organisms
Actinomyces
Enterococcus faecium
Listeria monocytogenes

Aerobic Gram-negative micro-organisms
Stenotrophomonas maltophilia

Anaerobic micro-organisms
Excepted as listed above

Other micro-organisms
Mycoplasma genitalium
Ureaplasma urealyticum

* Clinical efficacy has been demonstrated for susceptible isolates in the approved Indications.
+ Resistance rate ≥ 50% in one or more EU countries
($): Natural intermediate susceptibility in the absence of acquired mechanism of resistance
(1): In experimental studies with inhalation of Bacillus anthracis spores, it has been shown that antibiotic treatment starting early after exposure can prevent outbreak of the disease if treatment is designed so that the number of spores is below 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 an intravenous infusion of ciprofloxacin the mean maximum serum concentrations were achieved at the end of infusion. The pharmacokinetics of ciprofloxacin were linear over the dose range up to 400 mg when administered intravenously.

Comparison of the pharmacokinetic parameters for twice daily and three times daily intravenous dose regimen indicated no evidence of drug accumulation for ciprofloxacin and its metabolites.
A 60-minute intravenous infusion of 200 mg ciprofloxacin or the oral administration of 250 mg ciprofloxacin, both given every 12 hours, produced an equivalent area under the serum concentration time curve (AUC).
A 60-minute intravenous infusion of 400 mg ciprofloxacin every 12 hours was bioequivalent to a 500 mg oral dose every 12 hours with regard to AUC.
The 400 mg intravenous dose administered over 60 minutes every 12 hours resulted in a C_{max} similar to that observed with a 750 mg oral dose.
A 60-minute infusion of 400 mg ciprofloxacin every 8 hours is equivalent with respect to AUC to 750 mg oral regimen given 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 tissue (epithelial fluid, alveolar macrophages, biopsy tissue), paranasal sinuses, inflamed lesions (cantharides blister fluid), and 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 (M1), sulphociprofloxacin (M2), oxociprofloxacin (M3) and
formylciprofloxacin (M4). 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.

Excretion of ciprofloxacin (as % of dose)		
	Intravenoususe	
	Urine	**Faeces**
Ciprofloxacin	61.5	15.2
Metabolites (M1-M4)	9.5	2.6

Renal clearance is between 180-300 mL/kg/h and the total body clearance is 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 hours.

Non-renal clearance of ciprofloxacin is mainly due to active trans-intestinal secretion and metabolism. 1% of the dose is excreted via the bile. Ciprofloxacin is present in the bile in high concentrations.

Paediatric patients
Only limited pharmacokinetic data are available in paediatric patients.

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 hazard for humans based on conventional studies of single dose toxicity, repeated dose toxicity, carcinogenic potential and toxicity to reproduction.

Like many other quinolones, ciprofloxacin is phototoxic in animals at clinically relevant exposure levels. Data on photomutagenicity/ photocarcinogenicity show a weak photomutagenic or photocarcinogenic effect of ciprofloxacin *in-vitro* and in animal trials. This effect was comparable with 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

Lactic acid (E270).
Sodium chloride.
Hydrochloric Acid (E507) for pH adjustment.
Water for injections.

6.2 Incompatibilities

Unless compatibility with other solutions/drugs has been confirmed, the infusion solution must always be administered separately. The visual signs of incompatibility are e.g. precipitation, clouding, and discoloration.

Incompatibility appears with all infusion solutions/drugs that are physically or chemically unstable at the pH of the solutions (e.g. penicillins, heparin solutions), especially in combination with solutions adjusted to an alkaline pH (pH of ciprofloxacin solutions: 3.9 – 4.5).

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

Unopened:
Three years.
Single dose container.
From a microbiological point of view, the product should be used immediately once opened (see section 6.4).

6.4 Special precautions for storage

Polypropylene bag
Unopened:
Store below 25ºC. Keep the bag in the outer carton in order to protect from light.
Do not refrigerate or freeze.

Polypropylene bottles

Unopened:
Store below 25ºC.
Do not refrigerate or freeze.

Overwrapped bottles: Keep the bottles in the outer pouch in order to protect from light. To be used immediately after removing from the pouch (see section 6.3).

Bottles without overwrapping should be kept in the carton in order to protect from light. To be used immediately after removing from the carton (see section 6.3).

Since Ciprofloxacin 2 mg/ml Solution for infusion is light-sensitive, the bags and bottles should always be stored in the outer container. No special precautions are required during the normal 60 minute infusion period.

Do not refrigerate or freeze Ciprofloxacin 2 mg/ml Solution for infusion. If the product is inadvertently refrigerated, crystals may form. Do not use if crystals are present. These crystals will, however, redissolve at room temperature and do not adversely affect the quality of the product.

6.5 Nature and contents of container

100 ml polypropylene bags:
Plastic bags of polypropylene of 100 ml, with rubber (type I) closures, and
Aluminium caps with plastic flip-top covers. The bags are placed in cartons.
Packs of 10 bags are available.

100 ml polypropylene bottles:
Plastic bottles of polypropylene of 100 ml, with a molded plastic cap, a rubber (type II) gasket and a pull ring, or a twin port cap, which includes a rubber gasket (Type II) on the inside and two pull rings in the outside. Each bottle is placed in a metalized plastic pouch. The bottles are placed in cartons.
Packs of 10 or 20 bottles are available.

Alternatively:
Plastic bottles of polypropylene of 100 ml, with a molded plastic cap, a rubber (type II) gasket and a pull ring, or a twin port cap, which includes a rubber gasket (Type II) on the inside and two pull rings in the outside. The bottles are placed in cartons.
Packs of 10 or 20 bottles are available.

200 ml polypropylene bags:
Plastic bags of polypropylene of 200 ml, with rubber (type I) closures, and Aluminium caps with plastic flip-top covers. The bags are placed in cartons.
Packs of 5 bags are available.

200 ml polypropylene bottles:
Plastic bottles of polypropylene of 200 ml, with a molded plastic cap, a rubber (type II) gasket and a pull ring, or a twin port cap, which includes a rubber gasket (Type II) on the inside and two pull rings in the outside. Each bottle is placed in a metalized plastic pouch. The bottles are placed in cartons.
Packs of 10 or 20 bottles are available.

Alternatively:
Plastic bottles of polypropylene of 200 ml, with a molded plastic cap, a rubber (type II) gasket and a pull ring, or a twin port cap, which includes a rubber gasket (Type II) on the inside and two pull rings in the outside. The bottles are placed in cartons.
Packs of 10 or 20 bottles are available.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Intravenous infusion:

Ciprofloxacin should not be mixed with other drug products which are chemically or physically unstable at pH of 3.9 - 4.5 (see section 6.2).

The solution should be clear. Do not use if particles are present.
Ciprofloxacin is compatible with the following commonly used infusion fluids: Ringer's solution, Ringer lactate solution, 0.9% Sodium chloride solution, Dextrose 5% and Dextrose 10% solutions, Fructose 10% solution Sodium chloride 0.45% + Dextrose 5% solution and Sodium chloride 0.225% + Dextrose 5% solution. All solutions are stable for 48 hours below 25°C, with the only exception of the mixture of Ciprofloxacin with Ringer solution, which is stable for 12 hours below 25°C.

Unless compatibility is proven, the infusion solution should always be administered separately.

Since the infusion solution is photosensitive, the infusion bags and infusion bottles should be removed from the outer containeronly immediately before use.
Any unused solution should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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