CIPROLON® Infusion

(Ciprofloxacin)

ACTION

Ciprofloxacin, the active ingredient of Ciprolon, belongs to the quinolone group of substances. The main site of action of quinolones is a bacterial enzyme (gyrase) which plays a vital role in bacterial metabolism and reproduction. Blocking this enzyme with ciprofloxacin (a gyrase inhibitor) has a bactericidal effect on the disease pathogens (i.e. it kills the germs).

INDICATIONS

Adults

For the treatment of infections caused by organisms susceptible to ciprofloxacin: -

Infections:

- of the respiratory tract. Many of the organisms known as "problem germs" (e.g. Klebsiella, Enterobacter, Proteus, Pseudomonas, Legionella, Staphylococcus, Escherichia coli) react very sensitively to Ciprolon. Most cases of pneumonia which do not require hospital treatment are caused by *Streptococcus pneumoniae*. In such cases Ciprolon is not the drug of first choice.
- of the middle ear (otitis media) and the paranasal sinuses (sinusitis), particularly when they are caused by problem germs such as Pseudomonas or Staphylococcus. A different antibiotic should be used for acute tonsillitis.
- of the eyes
- of the kidneys and/or efferent urinary tract
- of the reproductive organs, inducing inflammation of the ovaries and fallopian tubes (adnexitis), gonorrrhoea and infections of the prostate gland (prostatitis)

Ciprolon is not effective against *Treponema pallidum* (the causative organism in syphilis).

- of the abdominal cavity, e.g. the gastrointestinal tract, the biliary tract and peritoneum (peritonitis)
- of the skin and soft tissues
- of the bones and joints.
- Blood poisoning (sepsis)
- Infections or the risk of infection (prophylaxis) in patients with a compromised immune system, e.g. who are being treated with drugs that suppress the body's natural immune defenses (immunosuppressants) of whose blood contains a reduced number of certain white blood cells (neutropenia).

For children and adolescents aged between 5 and 17:

- For acute infection episodes of cystic fibrosis (mucoviscidosis, an inherited metabolic disorder with increased production and increased viscosity of glandular secretions in the bronchi and digestive tract) caused by *P. aeruginosa*, provided that more effective parenteral treatment options do not appear practicable. Ciprolon is not recommended for other indications.

Anthrax:

- For immediate therapy and for treatment of anthrax following inhalation of anthrax (*Bacillus anthracis*). The efficacy; of Ciprolon in anthrax has been confirmed in studies.

DOSAGE AND ADMINISTRATION

Unless otherwise prescribed, the following doses are recommended (Table 1):

Adults

Indications	Single dose/ Frequency Quantity of active ingredient (mg ciprofloxacin)
Respiratory tract infections (depending on the severity and pathogen)	200-400 q 12 hrs
Complicated infections of the urinary tract	200 q 12 hrs
Diarrhoea	200 q 12 hrs
Other infections	200-400 q 12 hrs
Patients with particularly severe, life-threatening infections, especially those involving Pseudomonas, Staphylococcus or Streptococcus, e.g. pneumonia caused by Streptococcus	400 q 8 hrs
Recurrent infection episodes in mucoviscidosis patients (an inherited metabolic disorder with increased production and increased viscosity of glandular secretions in the bronchi and digestive tract)	400 q 8 hrs
Infections of bones and joints	400 q 8 hrs
Blood poisoning (sepsis)	400 q 8 hrs
Infections of the peritoneum (peritonitis)	400 q 8 hrs
Anthrax	400 q 12 hrs

Anthrax:

Children: 10 mg/kg body weight twice daily.

The maximum single dose for children must not exceed 400 mg.

Treatment should commence immediately after the suspected or confirmed inhalation of anthrax pathogens.

Note: In addition to Ciprolon, other infusion solutions containing lower and higher doses of the active ingredient are available for intravenous therapy, and other delivery forms are available for oral therapy.

Intravenous administration can be followed by further treatment on an oral basis.

Elderly patients

Elderly patients should receive as lowa dose as is compatible with the severity of the infection and their kidney function (creatinine clearance).

Children and adolescents

The recommended dose for acute infection episodes caused by P. aeruginosa in mucoviscidosis patients (an inherited metabolic disorder with increased production and increased viscosity of glandular secretions in the bronchi and digestive tract) is 3 x daily 10 mg/kg i.v. (maximum 1,200 mg/day).

Patients with impaired renal and heoatic function:

Adults

1. The following doses are recommended for moderate to severe impairment of renal function:
   - For patients with a creatinine clearance between 31 ml/min and 60 ml/min (serum creatinine between 1.4 mg/100 ml and 1.9 mg/ 100 ml), the maximum dose for intravenous administration is 800 mg ciprofloxacin per day.
   - For patients with a creatinine clearance 30 ml/min (serum creatinine >= 2 mg/100 ml), the maximum dose for intravenous administration is 400 mg ciprofloxacin per day.
2. Patients with impaired renal function who are undergoing haemodialysis should receive the same dose after each dialysis session as patients with moderate to severe impairment of renal function (see point 1).
3. patients with impaired renal function who use continuous ambulatory peritoneal dialysis (CAPO), Ciprolon infusion solution can be added to the (intraperitoneal) dialysate 4 x daily at 6-hour intervals at a dosage of 50 mg ciprofloxacin per litre dialysate for peritonitis.

There is only limited clinical experience involving a small number of patients in this indication. High doses of Ciprolon should be used in order to attain sufficiently high concentrations of ciprofloxacin in the peritoneum. As a result, patients must be closely monitored for side effects. If clinically relevant side effect or symptoms of an overdosage occur, the dosage must be lowered or use of Ciprolon discontinued.

4. It is not necessary to adjust the dosage for patients with impaired hepatic function.
5. In patients with impaired renal and hepatic function, the dosage should be adjusted as for impaired renallunction; it may be necessary to monitor the concentration of ciprofloxacin in the blood.

Children and adolescents

No information is available on the influence of impaired renal and hepatic function on the dosage for children and adolescents.

WARNINGS

The infusion time is 30 minutes for 1 bottle containing 100 ml infusion solution equivalent to 200 mg ciprofloxacin or 60 minutes for the infusion bag containing 200 ml infusion solution equivalent to 400 mg ciprofloxacin.

Ciprolon can be administered either directly or after being mixed with the compatible infusion solutions specified below.

Ciprolon is compatible with the following infusion solutions:

Physiological saline solution, Ringer solution and Ringer Lactate solution, 5% and 10% glucose solutions.

For how long should you use Ciprolon?

The duration of treatment depends on the severity of the infection and the clinical and bacteriological course. In general, therapy should always be continued systematically for at least 3 days after the fever has subsided and the clinical signs have disappeared. As a rule the average duration of treatment is:

Adults

- up to 7 days for infections of the kidneys, urinary tract and abdominal cavity,
- in patients with a compromised immune system, therapy should be continued for as long as the total white blood cell count is depressed (neutropenic phase),
- a maximum of 2 months for inflammation of the bone marrow (osteomyelitis),
- 7-14 days for all other infections.

In streptococcal infections therapy should be continued for at least 10 days because of the risk of late complications.

Chlamydia infections should likewise be treated for at least 10 days.

For children and adolescents aged between 5 and 17

10 - 14 days for acute infection episodes of cystic fibrosis caused by P. aeruginosa.

Anthrax

- 60 days of treatment for immediate therapy and for treatment of infections following inhalation of anthrax pathogens.

Please consult your doctor or pharmacist if you have the impression that the effects of Ciprolon are too strong or too weak.

If you have taken a greater quantity of Ciprolon than you were supposed to:

A few cases of transient (reversible) kidney damage have been reported following extremely large overdoses. In such cases, therefore, kidney function should be checked by a doctor.

PRECAUTIONS

Ciprolon must not be used:

- if you are hypersensitive (allergic) to ciprofloxacin or other drugs from the same substance group (quinolone type, gyrase inhibitor.
- if you are pregnant or breast-feeding.

Particular caution is required when using Ciprolon

If you suffer from seizures (epilepsy) or any other form of prior damage to the central nervous system (e.g. an increased tendency to seizures, a history of seizures, reduced blood flow in the brain, altered brain structure or a stroke in the past). Patients in this category are at risk of side effects in the central nervous system. In isolated cases, psychotic reactions (psychological impairment with altered perception ranging up to the point of self engagement) occurred, in some cases after first use. In these cases, stop using Ciprolon immediately and inform the attending doctor.

If severe and persistent diarrhoea develops during or after therapy. A doctor should be consulted in such cases as this may be a sign of a serious, possibly life-threatening intestinal disease (pseudomembranous colitis) which requires immediate treatment Use of Ciprolon must be discontinued in this case and suitable therapy should be implemented (e.g. vancomycin oral, 4 x 250 mg daily). Do not take drugs that inhibit gastric motility (peristalsis).

In isolated cases, inflammation of tendons (tendinitis) and rupturing of tendons (e.g. the Achilles tendon) have been observed following Treatment with fluoroquinolones (the substance group to which Ciprolon belongs). These occurrences were mainly observed in elderly patients who had been previously treated with corticosteroids. If inflammation of a tendon is suspected, treatment with Ciprolon must be discontinued immediately, physical strain must be avoided and appropriate therapy may have to be given.

Although photosensitivity only occurs very rarely following treatment with ciprofloxacin, patients undergoing treatment with Ciprolon should not be exposed unnecessarily to sunlight and should avoid exposure to UV light (high-altitude sun, solariums). Treatment must be discontinued in light sensitivity reactions (e.g. skin reactions similar to sunburn) are observed.

In isolated cases, severe immediate allergic reactions occurred involving swelling (oedema) of the face, blood vessels and larynx and difficulty in breathing (dyspnoea) ranging up to life-threatening shock (anaphylactic/ anaphylactoid reactions), in some cases after first use of the product. In these cases, stop using Ciprolon immediately and inform the attending doctor.

If consumption of sodium chloride could represent a risk factor for you for medical reasons, for example because you suffer from congestive heart failure, impaired kidney function or other kidney disorders (nephrotic syndrome), the additional burden of the sodium in this product must be taken into account. 1 bottle of 100 ml infusion solution contains 900 mg sodium chloride (15.5 mmol).

Children and adolescents

In common with other gyrase inhibitors, ciprofloxacin, the active ingredient in Ciprolon, is known to cause damage to the weight-bearing joints of juvenile animals. Evaluation of the safety data of patients aged less than 18 who were mainly suffering from cystic fibrosis (mucoviscidosis) did not reveal evidence of joint/cartilage damage.

Current findings support the use of Ciprolon for treatment of acute infection episodes of cystic fibrosis caused by P. aeruginosa in children and adolescents aged between 5 and 17; at present, only inadequate experience is available in regard to as use in children and adolescents with other infections and children aged less than 5. Ciproflxacin should therefore not be used lor other infections and not for children aged less than 5 in general.

Pregnancy

Ciprolon must not be used at any stage during pregnancy because no experience has been gained regarding use safety in pregnant women. Animal experiments have not produced any evidence of malformation of the foetus (teratogenic effects), but it is not entirely improbable that damage to cartilage may be caused in organisms which have not reached maturity.

Breast-feeding

It is also recommended on principle that Ciprolon should not be used while breasl-feeding. Driving and operating machinery:

Do not drive or operate power tools or machinery while taking this medicine; even when used correctly, this medicine may impair reaction speed so much that the ability to drive, operate machinery or work without a secure foothold may be reduced, or the patient may not be capable of doing these things at all. This applies particularly at the start of treatment, when the dose is increased, when medication is changed and in conjunction with alcohol.

SIDE EFFECTS

Like all medicines, Ciprolon can have side effects. The frequency is indicated as follows:

Frequently	≥ 1 %	to < 10 %
Occasionally	≥ 0.1 %	to < 1 %
Rarely	≥0.01 %	to < 0.1 %
Very rarely		< 0.01 %

General

Occasionally: A sensation of weakness. Long-term or repeated use of Ciprolon can reduce the susceptibility of disease- causing organisms to ciprofloxacin; this means that the patient may become infected again by the same organism or yeast-like organisms before the initial infection has been eradicated.

Rarely: Allergic reactions, drug fever, hypersensitivity reactions (anaphylactic/anaphylactoid reactions, e.g. facial, vascular and laryngeal oedema; dyspnoea ranging up to life-threatening shock), in some instances after the first administration; pain (e.g. pain in the limbs, back, chest).

Very rarely: Reactions similar to those associated with serum sickness (with, for example, fever, swelling of the lymph nodes, reddening of the skin, urticaria, swelling [oedema]), worsening of the symptoms of myasthenia gravis (load-related fatigue of the muscular system, particularly the muscles of the face, pharynx and respiratory tract).

Central nervous system

Occasionally: Headache, dizziness, fatigue, insomnia, agitation, contusion.

Rarely: Hallucinations, sweating, peripheral paraesthesia, anxiety, nightmares, depression, tremor, convulsions, decreased sensitivity to touch.

Very rarely: Unsteady gait, increased intracranial pressure, psychotic reactions (psychological impairment with altered perception ranging up to the point of self-endangerment), in some cases after first use, impaired coordination, increased sensitivity to touch, increased muscular tone, muscular twitching.

Gastrointestinal tract Frequently: Nausea, diarrhoea.

Occasionally: Vomiting, impaired digestion, abdominal pain, flatulence, loss of appetite.

Rarely: Jaundice, pseudomembranous colitis.

Very rarely: Liver damage (hepatitis, liver cell necrosis ranging up to life-threatening liver failure), pancreatitis.

Cardiovascular

Rarely: Palpitations, migraine, unconsciousness, hot flushes, swelling in legs (peripheral oedema), low blood pressure.

Blood

Occasionally: Increased levels of a certain type of white blood cell (eosinophilia), reduced levels of white blood cells (leucocytopenia).

Rarely: Reduced levels of red or certain white blood cells (anaemia, granulocytopenia) or blood platelets (thrombocytopenia), increased levels of white blood cells (leukocytosis) or blood platelets (thrombocytosis), changed blood coagulation factors (prothrombin values).

Very rarely: Increased degradation of red blood corpuscles (haemolytic anaemia), a reduction in all blood cells (pancytopenia, possibly life-threatening), a severe decrease in a certain type of white blood cell with the possible symptoms of shivering, fever, blisters in the oral and throat mucosa (agranulocytosis), reduced bone marrow function (possibly life-threatening).

Locomotor system Occasionally Joint pain.

Rarely: Muscle pain, swelling in the joints.

Very rarely: Inflammation of the tendons (tendinitis), inflammation of the tendon sheath (tendovaginitis) and torn tendons (e.g. the Achilles tendon), muscular weakness (myasthenia).

Skin

Frequently: Skin rash.

Occasionally: Itching (pruritus), raised, spotty skin rash (maculopapular exanthema), nettle rash (urticaria).

Rarely: Light sensitivity with reddening of the skin (photosensitivity).

Very rarely: Punctate skin haemorrhages (petechiae), blister formation with accompanying haemorrhages (haemorrmagic bullae) and small nodules (papules) with crust formation showing vascular involvement (vasculitis), erythema nodosum, rash on the skin and mucous membranes close to the skin (fixed drug-induced exanthem), erythema exsudativum multiforme (minor) ranging up to severe forms (Stevens-Johnson syndrome), blister-like loss of the skin and oral/nasal mucosa (Lyell's syndrome).

Sensory organs:

Occasionally: Impaired sense of taste and smell.

Rarely: Tinnitus, transient loss of hearing, particularly with high tones, visual disturbances (e.g. double vision, coloured vision), loss of the sense of taste which is usually reversible after discontinuation of therapy.

Very rarely: Loss of the sense of smell which is usually reversible after discontinuation of therapy.

Urogenital tract

Rarely: Inflammation of the kidney (interstitial nephritis), transient impairment in kidney function ranging up to transient kidney failure.

Laboratory findings

Occasionally: Particularly in patients with pre-existing liver damage, temporary effect on liver function with an increase in liver enzymes (transaminases, alkaline phosphatase) ranging up to jaundice; transient increase in the levels of urea, creatinine and bilirubin (a bile pigment) in the blood.

Rarely: Raised levels of blood glucose (hyperglycaemia) and blood or crystals in the urine (haematuria and crystalluria).

Very rarely: Increased levels of certain enzymes (amylase, lipase).

Reactions at the injection site

Occasionally: Venous inflammation (phlebitis), local reactions at the injection site.

Inform your doctor or pharmacist if you notice any side effects that are not listed in this patient information leaflet.

Drug Interactions

Ciprolon must be administered separately unless compatibility with other infusion solutions/drug products has been confirmed. Visible signs of incompatibility include precipitation, cloudiness and discoloration of the solution. Incompatibility appears with all infusion solutions/drug products that are physically or chemically unstable at the pH of Ciprolon (e.g. penicillins, heparin solutions), particularly when combined with solutions adjusted to an alkaline pH (pH of Ciprolon infusion solution: 3.9 - 4.5).

Ciprolon/xanthines

Taking Ciprolon and theophylline (an asthma treatment) at the same time can lead to an unwanted increase in the concentration of theophylline in the blood and, accordingly, to an increase in the rate of side effects caused by theophylline which, in isolated cases, may be life-threatening or fatal. If it is imperative to use both medicines at the same time, the theophylline concentration in the blood should be monitored and the dosage should be reduced as required. There have been reports of raised concentrations of the xanthine derivatives caffeine and pentoxifylline (a medicine that promotes blood circulation) in the blood when these substances are administered at the same time as Ciprolon .

Ciprolon/non-steroidal anti-inflammatory drugs

Animal studies have shown that using a combination of very high doses of quinolones (gyrase inhibitors) and certain drugs, which inhibit inflammation (non-steroidal anti-inflammatory agents) can trigger seizures. This does not apply to medicine containing acetylsalicylic acid.

Ciprolon/cyclosporin

Temporary impairment of kidney function associated with an increase in the concentration of creatinine in the blood ha been observed in isolated cases when Ciprolon is taken at the same time as cyclosporin (a drug that suppresses the body's defence mechanisms). Your creatinine concentration should be monitored closely (twice a week) if you are taking both medicines at the same time.

Ciprolon/warfarin

Simultaneous use of Ciprolon and warfarin (a drug that inhibits the coagulation of blood) may increase the action of warfarin.

Ciprolon/glibenclamide

In isolated cases, concomitant use of Ciprolon and glibenclamide (a treatment for diabetes) may increase the action of glibenclamide to such an extent that hypoglycaemia may occur.

Ciprolon/probenecid

Probenecid (a treatment for gout) affects the excretion of ciprofloxacin in urine (renal secretion). Simultaneous use of Ciprolon and probenecid increases the concentration of ciprofloxacin in the blood (serum).

Ciprolon/metoclopramide

Metoclopramide (a gastrointestinal medicine) accelerates the absorption of Ciprolon into the blood and causes the maximum concentration in the blood (plasma) to be reached more rapidly than usual. No effect on the bioavailability, Ciprolon in the human body has been observed.

Ciprolon/mexiletine

Simultaneous use of these two medicines may lead to a raised concentration of mexiletine in the body.

Ciprolon/phenytoin

Elevated or lowered serum concentrations of phenytoin have been reported following the simultaneous use of these two medicines.

Ciprolon/diazepam

There have been reports that concomitant use of Ciprolon and diazepam delays the decomposition of diazepam in the body (reduced clearance, extended half-life). Accordingly, careful monitoring of diazepam treatment is recommended.

Ciprolon/methotrexate

Simultaneous use of these two substances can lead to delayed excretion of methotrexate and thus to increased plasma levels of methotrexate. These patients should be carefully monitored, as this condition can lead to an increased risk of the reactions induced by methotrexate.

Ciprolon/omeprazole

Concomitant administration of ciprofloxacin with omeprazole can lead to a slight reduction in the peak plasma levels (Cmax) and bioavailability (AUC) of ciprofloxacin.

Please inform your doctor or pharmacist if you are taking other medicines or have taken other medicines recently, ever they are non-prescription medicines.

STORAGE

Store below 30°C, protect from freezing. The solution is light sensitive.

PRESENTATIONS

Vials

CIPROLON 200: Ciprofloxacin (as lactate) 200 mg in 100 ml/ vial

Infusion bags

CIPROLON 400: Ciprofloxacin (as lactate) 400 mg in 200 ml/ infusion bag

Excipients: Lactic acid, Sodium Chloride, Hydrochloric acid, Water for Injection

THIS IS A MEDICAMENT

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous.
- Follow the doctor's prescription strictly, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

Manufactured by:
Hikma Farmacêutica, Portugal
For: HIKMA Pharmaceuticals, Amman-Jordan

Keep medicament out of the reach of children

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