PARVENS

Instructions for the medicinal product

Trade name: Parvens.
International Nonproprietary Name: Ciprofloxacin + Sodium Chloride.
Dosage form: Solution for Infusion.
Composition: Each 100 ml contains:

Ciprofloxacin USP	200 mg;
Sodium Chloride BP	900 mg;
Water for injections BP	q.s.

Pharmacotherapeutic group: Fluoroquinolones.
ATC Code: J01MA02.
Pharmacologic property:
Pharmacodynamics:
Ciprofloxacin has in vitro activity against a wide range of gram-negative and gram-positive microorganisms. The bactericidal action of ciprofloxacin results from inhibition of the enzymes topoisomerase II (DNA gyrase) and topoisomerase IV, which are required for bacterial DNA replication, transcription, repair, and recombination. The mechanism of action of fluoroquinolones, including ciprofloxacin, is different from that of penicillins, cephalosporins, aminoglycosides, macrolides, and tetracyclines; therefore, microorganisms resistant to these classes of drugs may be susceptible to ciprofloxacin and other quinolones. There is no known cross-resistance between ciprofloxacin and other classes of antimicrobials. In vitro resistance to ciprofloxacin develops slowly by multiple step mutations.
Ciprofloxacin has been shown to be active against most isolates of the following bacteria:
Gram-positive bacteria: Enterococcus faecalis, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus saprophyticus, Streptococcus pneumoniae, Streptococcus pyogenes.
Gram-negative bacteria: Campylobacter jejuni, Proteus mirabilis, Citrobacter diversus, Proteus vulgaris, Citrobacter freundii, Providencia rettgeri, Enterobacter cloacae, Providencia stuartii, Escherichia coli, Pseudomonas aeruginosa, Haemophilus influenzae, Salmonella typhi, Haemophilus parainfluenzae, Serratia marcescens, Klebsiella pneumoniae, Shigella boydii, Moraxella catarrhalis, Shigella dysenteriae, Morganella morganii, Shigella flexneri, Neisseria gonorrhoeae, Shigella sonnei.
Ciprofloxacin has been shown to be active against Bacillus anthracis both in vitro and by use of serum levels as a surrogate marker.
Pharmacokinetics:
Following an intravenous infusion of ciprofloxacin the mean maximum serum concentrations were achieved at the end of infusion. Pharmacokinetics of ciprofloxacin were linear over the dose range up to 400 mg administered intravenously.
Comparison of the pharmacokinetic parameters for a twice a day and three times a day 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 Cmax 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.
Protein binding of ciprofloxacin is low (20-30%). Ciprofloxacin is present in plasma largely in a non-ionised form and has a large steady state distribution volume of 2-3 L/kg body weight. Ciprofloxacin reaches high concentrations in a variety of tissues such as lung (epithelial fluid, alveolar macrophages, biopsy tissue), sinuses, inflamed lesions (cantharides blister fluid), and the urogenital tract (urine, prostate, endometrium) where total concentrations exceeding those of plasma concentrations are reached.
Indications for use:
The Parvens is indicated for the treatment of the following infections. Special attention should be paid to available information on resistance to ciprofloxacin before commencing therapy.
Adults:
Lower respiratory tract infections due to Gram-negative bacteria:
- Exacerbations of chronic obstructive pulmonary disease;
- Broncho-pulmonary infections in cystic fibrosis or in bronchiectasis, pneumonia;
- Chronic suppurative otitis media;

Acute exacerbation of chronic sinusitis especially if these are caused by Gram-negative bacteria:
- Urinary and genital tract infections;
- Gonococcal uretritis and cervicitis due to susceptible Neisseria gonorrhoeae;
- Epididymo-orchitis including cases due to susceptible Neisseria gonorrhoeae;
- Pelvic inflammatory disease including cases due to susceptible Neisseria gonorrhoeae;
- Infections of the gastro-intestinal tract (e.g. travellers' diarrhoea);
- Intra-abdominal infections;
- Infections of the skin and soft tissue caused by Gram-negative bacteria;
- Malignant external otitis;
- Infections of the bones and joints;
- Prophylaxis of invasive infections due to Neisseria meningitidis;
- Inhalation anthrax (post-exposure prophylaxis and curative treatment).
- Ciprofloxacin may be used in the management of neutropenic patients with fever that is suspected to be due to a bacterial infection.

Children and adolescents:
- Broncho-pulmonary infections in cystic fibrosis caused by Pseudomonas aeruginosa;
- Complicated urinary tract infections and pyelonephritis;
- Inhalation anthrax (post-exposure prophylaxis and curative treatment);
- Parvens may also be used to treat severe infections in children and adolescents when this is considered to be necessary.

Treatment should be initiated only by physicians who are experienced in the treatment of cystic fibrosis and/or severe infections in children and adolescents.
Parvens is not a drug of first choice in the pediatric population due to an increased incidence of adverse events compared to controls, including events related to joints and/or surrounding tissues.
Contraindications:
- Hypersensitivity to the active substance, to other quinolones or to any of the excipients;
- Concomitant administration of ciprofloxacin and tizanidine;
- Pediatric patients (less than 18 years of age). The use of Parvensn in children and adolescents should follow available official guidance;
- Pregnancy and lactation.

With caution: Severe cerebral atherosclerosis, cerebrovascular accidents, mental illness, epilepsy, epileptic syndrome, marked renal and/or hepatic impairment, advanced age.
Pregnancy and lactation:
As a precautionary measure, it is preferable to avoid the use of ciprofloxacin during pregnancy.
Ciprofloxacin is excreted in breast milk. Due to the potential risk of articular damage, ciprofloxacin should not be used during breast-feeding.
Dosage and directions for use:
Adults:
Infections of the lower respiratory tract: 400 mg twice daily to 400 mg three times a day. Total duration of treatment - 7 to 14 days.
Infections of the upper respiratory tract:
Acute exacerbation of chronic sinusitis - 400 mg twice daily to 400 mg three times a day. Total duration of treatment - 7 to 14 days.
Chronic suppurative otitis media - 400 mg twice daily to 400 mg three times a day. Total duration of treatment - 7 to 14 days.
Malignant external otitis - 400 mg three times a day. Total duration of treatment - 28 days up to 3 months.
Urinary tract infections:
Complicated and uncomplicated pyelonephritis - 400 mg twice daily to 400 mg three times a day. Total duration of treatment - 7 to 21 days, it can be continued for longer than 21 days in some specific circumstances (such as abscesses).
Prostatitis - 400 mg twice daily to 400 mg three times a day. Total duration of treatment - 2 to 4 weeks (acute).
Genital tract infections:
Epididymo-orchitis and pelvic inflammatory diseases - 400 mg twice daily to 400 mg three times a day. Total duration of treatment - at least 14 days.
Infections of the gastro-intestinal tract and intra-abdominal infections:
Diarrhoea caused by bacterial pathogens including Shigella spp. other than Shigella dysenteriae type 1 and empirical treatment of severe travellers' diarrhea - 400 mg twice daily. Total duration of treatment - 1 day.
Diarrhoea caused byShigella dysenteriae type 1 - 400 mg twice daily. Total duration of treatment - 5 days.
Diarrhoea caused byVibrio cholera - 400 mg twice daily. Total duration of treatment - 3 days.
Typhoid fever - 400 mg twice daily. Total duration of treatment - 7 days.
Intra-abdominal infections due to Gram-negative bacteria - 400 mg twice daily to 400 mg three times a day. Total duration of treatment - 5 to 14 days.
Infections of the skin and soft tissue: 400 mg twice daily to 400 mg three times a day. Total duration of treatment - 7 to 14 days.
Bone and joint infections: 400 mg twice daily to 400 mg three times a day. Total duration of treatment - max. of 3 months.
Neutropenic patients with fever that is suspected to be due to a bacterial infection: 400 mg twice daily to 400 mg three times a day. Total duration of treatment -Therapy should be continued over the entire period of neutropenia.
Parvens should be co-administered with appropriate antibacterial agent(s) in accordance to official guidance.
Inhalation anthrax post-exposure prophylaxis and curative treatment for persons requiring parenteral treatment: 400 mg twice daily. Total duration of treatment - 60 days from the confirmation of *Bacillus anthracis* exposure.
Drug administration should begin as soon as possible after suspected or confirmed exposure.
Paediatric population:
Cystic fibrosis: 10 mg/kg body weight three times a day with a maximum of 400 mg per dose. Total duration of treatment - 10 to 14 days.
Complicated urinary tract infections and pyelonephritis: 6 mg/kg body weight three times a day to 10 mg/kg body weight three times a day with a maximum of 400 mg per dose. Total duration of treatment - 10 to 21 days.
Inhalation anthrax post-exposure curative treatment for persons requiring parenteral treatment: 10 mg/kg body weight twice daily to 15 mg/kg body weight twice daily with a maximum of 400 mg per dose. Total duration of treatment - 60 days from the confirmation of *Bacillus anthracis* exposure.
Drug administration should begin as soon as possible after suspected or confirmed exposure.
Other severe infections: 10 mg/kg body weight three times a day with a maximum of 400 mg per dose. Total duration of treatment - According to the type of infections.
Elderly patients:
Elderly patients should receive a dose selected according to the severity of the infection and the patient`s creatinine clearance.
Patients with renal and hepatic impairment:
Recommended starting and maintenance doses for patients with impaired renal function:
Creatinine Clearance [mL/min/1.73 m²] - > 60, Serum Creatinine [µmol/L] - <124, Intravenous Dose [mg] -See usual Dose.
Creatinine Clearance [mL/min/1.73 m²] - 30- 60, Serum Creatinine [µmol/L] - 124 to 168, Intravenous Dose [mg] -200-400 mg every 12 h.
Creatinine Clearance [mL/min/1.73 m²] - <30, Serum Creatinine [µmol/L] - >169, Intravenous Dose [mg] -200-400 mg every 24 h.
Creatinine Clearance [mL/min/1.73 m²] - Patients on haemodialysis, Serum Creatinine [µmol/L] - >169, Intravenous Dose [mg] -200-400 mg every 24 h (after dialysis).
Creatinine Clearance [mL/min/1.73 m²] - Patients on peritoneal dialysis, Serum Creatinine [µmol/L] - >169, Intravenous Dose [mg] -200-400 mg every 24 h.
Parvens should be checked visually prior to use. It must not be used if cloudy.
Parvens should be administered by intravenous infusion. For children, the infusion duration is 60 minutes.
In adult patients, infusion time is 60 minutes for 400 mg Parvens and 30 minutes for 200 mg Parvens. Slow infusion into a large vein will minimise patient discomfort and reduce the risk of venous irritation.
Side-effects:
Infections and infestations: Uncommon: Mycotic superinfections. Rare: Antibiotic associated colitis (very rarely with possible fatal outcome).
Blood and lymphatic system disorders: Uncommon: Eosinophilia. Rare: leukopenia, anaemia, neutropenia, leukocytosis, thrombocytopenia, thrombocytaemia. Very rare: haemolytic anaemia, agranulocytosis, pancytopenia (life-threatening), bone marrow depression (life-threatening).
Immune system disorders: Rare: allergic reaction, allergic oedema / angiooedema. Very rare: anaphylactic reaction, anaphylactic shock (life-threatening), serum sickness-like reaction.
Metabolism and nutrition disorders: Uncommon: Anorexia. Rare: Hyperglycaemia.
Psychiatric disorders: Uncommon: Psychomotor hyperactivity / agitation. Rare: Confusion and disorientation, anxiety reaction, abnormal dreams, depression (potentially culminating in suicidal ideations/thoughts or suicide attempts and completed suicide), hallucinations. Very rare: Psychotic reactions (potentially culminating in suicidal ideations/thoughts or suicide attempts and completed suicide).
Nervous system disorders: Uncommon: headache, dizziness, sleep disorders, taste disorders. Rare: Par- and dysaesthesia, hypoesthesia, tremor, Vertigo. Very rare: migraine, disturbed coordination, gait disturbance, olfactory nerve disorders, intracranial hypertension. Frequency not known: Peripheral neuropathy.
Eye disorders: Rare: Visual disturbances (e.g. diplopia). Very rare: Visual colour distortions.
Ear and labyrinth disorders: Rare: Tinnitus, hearing loss / hearing impaired.
Cardiac disorders: Rare: Tachycardia. Frequency not known: Ventricular arrhythmia and torsades de pointes (reported predominantly in patients with risk factors for QT prolongation), ECG QT prolonged.
Vascular disorders: Rare: vasodilatation, hypotension, syncope. Very rare: vasculitis.
Respiratory, thoracic and meditational disorders: Rare: dyspnoea (including asthmatic condition).
Gastrointestinal disorders: Common: nausea, diarrhoea. Uncommon: vomiting, gastrointestinal and abdominal pains, dyspepsia, flatulence. Very rare: pancreatitis.
Hepatobiliary disorders: Uncommon: increase in transaminases, increased bilirubin. Rare: hepatic impairment, cholestatic icterus, hepatitis. Very rare: liver necrosis (very rarely progressing to life-threatening hepatic failure).
Skin and subcutaneous tissue disorders: Uncommon: rash, pruritus, urticaria. Rare: photosensitivity reactions. Very rare: petechiae, erythema multiforme, erythema nodosum
Stevens-Johnson syndrome (potentially life-threatening), toxic epidermal necrolysis (potentially life-threatening).
Musculoskeletal, connective tissue and bone disorders: Uncommon: musculoskeletal pain (e.g. extremity pain, back pain, chest pain), arthralgia. Rare: myalgia, arthritis, increased muscle tone and cramping. Very rare: muscular weakness, tendinitis, tendon rupture (predominantly Achilles tendon).
Renal and urinary disorders: Uncommon: renal impairment. Rare: renal failure, haematuria, crystalluria, tubulointerstitial nephritis.
General disorders and administration site conditions: Uncommon: asthenia, fever. Very rare: oedema, sweating (hyperhidrosis).
Overdose:
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.
Treatment: In the event of overdose, symptomatic treatment should be implemented. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation.
Drug interaction:
Effects of ciprofloxacin on other medicinal products:
Tizanidine - Tizanidine must not be administered together with ciprofloxacin.
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 xanthenes derivatives were reported.
Phenytoin - Simultaneous administration of ciprofloxacin and phenytoin may result in increased or reduced serum levels of phenytoin such that monitoring of drug levels is recommended.
Cyclosporin - A transient rise in the concentration of serum creatinine was observed when ciprofloxacin and cyclosporin containing medicinal products were administered simultaneously. Therefore, it is frequently (twice a week) necessary to control the serum creatinine concentrations in these patients.
Vitamin K antagonists - Simultaneous administration of ciprofloxacin with a vitamin K antagonist may augment its anti-coagulant effects. The risk may vary with the underlying infection, age and general status of the patient so that the contribution of ciprofloxacin to the increase in INR (international normalised ratio) is difficult to assess. The INR should be monitored frequently during and shortly after co-administration of ciprofloxacin with a vitamin K antagonist (e.g., warfarin, acenocoumarol, phenprocoumon, or fluindione).
Glibenclamide - In particular cases, concurrent administration of ciprofloxacin and glibenclamide containing medicinal products can intensify the action of glibenclamide (hypoglycaemia).
Ropinirole - 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 - Concomitant use of lidocaine containing medicinal products with ciprofloxacin, a moderate inhibitor of CYP450 1A2 isozyme, reduces clearance of intravenous lidocaine by 22%.
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.
Sildenafil - Caution should be used prescribing ciprofloxacin concomitantly with sildenafil taking into consideration the risks and the benefits.
Cautions:
Parvens 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.
Parvens is not recommended for the treatment of streptococcal infections due to inadequate efficacy.
Caution should be taken when using fluoroquinolones, including ciprofloxacin, in patients with known risk factors for prolongation of the QT interval.
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.
The use of Parvens in children and adolescents should follow available official guidance. Parvens treatment should be initiated only by physicians who are experienced in the treatment of cystic fibrosis and/or severe infections in children and adolescents.
Patients receiving Parvens should be well hydrated and excessive alkalinity of the urine should be avoided.
Ciprofloxacin has been shown to cause photosensitivity reactions. Patients taking Parvens should be advised to avoid direct exposure to either extensive sunlight or UV irradiation during treatment.
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.
Presentation:
1x1, 100 ml Plastic bottle in a monocarton, with instruction for use.
Storage:
Keep in dry place, protected from light at a temperature below 30°C. Keep out of reach of children. Do not freeze.
Shelf life:
Labeled. Do not use after expiry date.
Distribution Condition:
Prescribed medicine.

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SPEY

Manufactured for:
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Kabul, Afghanistan
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