xxxxxxxx-5253

QUINTOR 500 MG TABLETS

(Ciprofloxacin Tablets USP 500 mg)

Quintor (Ciprofloxacin) is a synthetic, fluoroquinolone derivative with bactericidal activity against a wide range of Gram-negative and Gram-positive organisms. It is indicated in infections by a number of Gram-negative and Gram-positive microbes, such as, respiratory tract infections, urinary tract infections, skin and soft tissue infections, osteomyelitis and sexually transmitted disease caused by susceptible microorganisms.

MODE OF ACTION:

In vitro studies have shown that the antibacterial action of Quintor (Ciprofloxacin) results from the inhibition of bacterial DNA gyrase.

Quintor (Ciprofloxacin) does not cross-react with penicillins, cephalosporins, aminoglycosides or tetracyclines and organisms resistant to these antibiotics are generally sensitive to Quintor (Ciprofloxacin).

ANTIBACTERIAL EFFECTS:

Quintor (Ciprofloxacin) is active against the following Gram-negative and Gram-positive organisms in vitro: E.coli. Shigella, Salmonella, Citrobacter, Klebsiella, Enterobacter, Serratia, Proteus (indole-positive and indole-negative), Providencia, Vibrio, Aeromonas, Pasteurella, Haemophilus, Gardnerella, Campylobacter, Pseudomonas, Legionella, Neisseria, Acinetobacter, Brucella, Streptococcus (including S.faecalis), Staphylococus, Corynebacterium, Fusobacterium, Actinomyces, Mycoplasma, Yersinia, Clostridium and Chlamydia.

In-vitro studies have shown that additive activity often results when Quintor (Ciprofloxacin) is combined with other antibacterial agents.

Synergism is observed occasionally but antagonism is rarely seen.

CLINICAL PHARMACOLOGY:

After oral administration of single doses of Quintor (Ciprofloxacin) peak serum concentrations of 0.28 to 5.92 mg/L were reached within 0.5 to 2 hours. Mean peak concentrations increased in proportion to the dose within the normal therapeutic range of 500 mg to 750 mg twice a day.

Multiple dose administration for up to 8 days in healthy volunteers did not produce significant drug accumulation. Food delays the absorption of Quintor (Ciprofloxacin) however; simultaneous administration of antacids containing magnesium hydroxide/ aluminium hydroxide with Quintor (Ciprofloxacin) reduces its bioavailability. The absolute bioavailability of oral Quintor (Ciprofloxacin) averages between 69 and 85%. The tissue concentrations achieved are at least as high as the serum concentrations for most tissues. Quintor (Ciprofloxacin) was approximately 16 to 40% bound to plasma proteins. The elimination half-life of Quintor (Ciprofloxacin) after single and multiple doses ranges from 3.4 to 6.9 hours following oral administration. Pharmacokinetics of Quintor (Ciprofloxacin) are altered in patients with renal dysfunction and dosage adjustment may be required in such subjects. Unchanged Quintor (Ciprofloxacin) is the major moiety in both urine (45%) and feces (25%). Small amounts of 4 metabolites are present in urine and feces and all of them possess some antibacterial activity. However, this is less than that of Quintor (Ciprofloxacin).

INDICATIONS

UNCOMPLICATED AND COMPLICATED-INFECTIONS CAUSED BY CIPROFLOXACIN SENSITIVE PATHOGENS:

Infections of the respiratory tract

In the treatment of outpatients with pneumonia-due to Pneumococcus ciprofloxacin should not be used as a first choice of drug. Ciprofloxacin can be regarded as an advisable treatment for pneumonias caused by Klebsiella, Enterobacter, Proteus, E Coli, Pseudomonas, Haemophilus Branhamella, Legionella, and Staphylococcus.

Infections of the middle ear (otitis media), of the paranasal sinuses (sinusitis), especially if these are caused by gram negative organisms including Pseudomonas or by Staphylococcus.

Infections of the eyes.

Infections of the kidneys and/or the efferent urinary tract.

Infections of the genital organs, including adnexitis, gonorrhoea, prostatitis.

Infections of the abdominal cavity (e.g. infections of the gastrointestinal tract or of the biliary tract, peritonitis).

Infections of the skin and soft tissue.

Infections of the bones and joints.

Sepsis

Infections or imminent risk of infection (prophylaxis) in patients whose immune system has been weakened (e.g. patients on immunosuppressant or have neutropenia).

Selective intestinal decontamination in immunosuppressed patients.

According to in-vitro investigations, the following pathogens can be regarded as sensitive:

E. coli, Shigella, Salmonella, Citrobacter, Klebsiella, Enterobacter, Serratia, Hafnia, Edwardsiella, Proteus (indole-positive and Indole-negative), Providencia, Morganella, Yersinia; Vibrio, Aeromonas, Plesiomonas, Pasteurella, Haemophilus, Campylobacter, Pseudomonas, Legionella, Neisseria Moraxella, Acinetobacter, Brucella; Staphylococcus, Listeria, Corynebacterium, Chlamydia.

The following show varying degrees of sensitivity:

Gardnerella, Flavobacterium, Alcaligenes, Streptococcus agalactiae, Enterococcus faecalis, Streptococcus pyogenes, Streptococcus pneumoniae Viridans group streptococci, Mycoplasma hominis, Mycobacterium tuberculosis, and Mycobacterium fortuitum.

The following are usually resistant:

Enterococcus faecium, Ureaplasma urealyticum, Nocardia asteroides.

With a few exceptions anaerobes are moderately sensitive e.g. Peptococcus, Peptostreptococcus to resistant e.g. Bacteroides.

Ciprofloxacin is ineffective against Treponema pallidum

CONTRAINDICATIONS:

Safety during pregnancy and lactation has not been established.

Quintor is contra-indicated in children under 18 years and in growing adolescents, except where the benefits of treatment exceed the risks.

Experimental evidence indicates that, species variable reversible lesions of the cartilage of weight bearing joints have been seen in immature members of certain animal species.

Quintor is contra-indicated in patients who have shown hypersensitivity to ciprofloxacin or any other quinolones.

WARNINGS AND PRECAUTIONS:

Nervous System:

In epileptics and in patients who have suffered from previous CNS-disorders (e.g. lowered convulsion threshold, previous history of convulsion, reduced cerebral blood flow, altered brain structure or stroke), ciprofloxacin should only be used where the benefits of treatment exceed the risks, since these patients are endangered because of possible central-nervous side effects.

In some instances the CNS reactions occurred after the first administration of Ciprofloxacin already. In rare case depression or psychosis can progress to self endangering behaviour, in these cases ciprofloxacin has to be discontinued and the doctor should be informed immediately.

Gastrointestinal System:

In the event of severe and persistent diarrhoea during or after treatment a doctor must be consulted, since this symptom can hide a serious intestinal disease (Life threatening pseudomembranous colitis with possible fatal outcome), requiring immediate treatment. In such cases Ciprofloxacin must be discontinued and appropriate therapy initiated.

Drugs that Inhibit peristalsis is contraindicated. There can be a temporary increase in transaminases, alkaline phosphates or Cholestatic jaundice, especially in patients with previous liver damage.

Hypersensitivity:

In some instances, the hypersensitivity and allergic reactions already occurred after the first administration and the doctor should be informed immediately.

Anaphylactic/anaphylactoid reactions in very rare instances can progress to a life threatening shock, in some Instances after the first administration. In these cases Ciprofloxacin has to be discontinued, medical treatment (e.g. treatment for shock) is required.

Musculo-skeletal system

The risk of developing fluoroquinolone-associated tendonitis and tendon rupture is further increased in people older than 60, in those taking corticosteroid drugs, and in kidney, heart and lung transplant recipients. Patients experiencing pain, swelling, inflammation of a tendon or tendon rupture should be advised to stop taking their fluoroquinolone medication (Ciprofloxacin) and to contact their health care professional promptly about changing their antimicrobial therapy.

Patients should also avoid exercise and using the affected area at the first sign of tendon pain, swelling or inflammation.

Exacerbation of myasthenia gravis:

Fluoroquinolones have neuromuscular blocking activity and may exacerbate muscle weakness in person with myasthenia gravis. Post marketing serious adverse events, including deaths and requirement for ventilator support have been associated with fluoroquinolones use in persons with myasthenia gravis. Avoid fluoroquinolones in patients with known history of myasthenia gravis.

Skin and appendages:

Ciprofloxacin has been shown to produce photosensitivity reactions.

Patients taking Ciprofloxacin should avoid direct exposure to excessive sunlight or UV-light. Therapy should be discontinued if photosensitation (i.e. sunburn-like skin reactions) occurs.

Ability to drive and use machines:

Even when the drug is taken exactly as prescribed, it can affect the speed of reaction to such an extent that the ability to drive or to operate machinery is impaired. This applies particularly in combination with alcohol.

Paediatric use: As with other drugs in its class, ciprofloxacin has been shown to cause arthropathy in weight-bearing joints of immature animals. Although analysis of available safety data from ciprofloxacin use in patients less than 18 years of age, the majority of whom had cystic fibrosis, did not disclose any evidence of drug-related cartilage or articular damage, its use in the paediatric population is generally not recommended.

Cytochrome P450 (CYP450): Ciprofloxacin is an inhibitor of the hepatic CYP1A2 enzyme pathway. Co-administration of ciprofloxacin and other drugs primarily metabolized by the CYP1A2 (e.g. theophylline, methylxanthines, tizanidine) results in increased plasma concentrations of the coadministered drug and could lead to clinically significant pharmacodynamic side effects of the coadministered drug.

Use in Pregnancy, Lactation and Children

Use of Quintor (Ciprofloxacin) during pregnancy is not recommended.

As Quintor (Ciprofloxacin) is secreted in milk, its administration to nursing mothers is also not recommended.

Quintor (Ciprofloxacin) has been shown to cause arthropathy in weight bearing joints of immature animals and so its use in children and growing adolescence is not recommended. However, where the benefit of using Quintor (Ciprofloxacin) is considered to out-weigh this potential risk, the dosage should be 7.5 to 15 mg/kg/day administered in two divided doses/day depending upon the severity of infections.

ADVERSE EFFECTS:

The most common adverse reactions which has been reported in clinical studies with Ciprofloxacin (Oral, Parenteral) sorted by body systems.

BODY SYSTEM	Adverse Drug Reactions
Incidence of frequency 1%<10%	
Digestive system	nausea, diarrhoea
Skin and appendages:	rash
Incidence of frequency 0.1%<1%	
Body as whole:	abdominal pain, moniliasis, asthenia (general feeling of weakness, tiredness)
Cardiovascular system	(thrombo)-phlebitis
Digestive system.	SGOT increased, SGPT increased, vomiting., dyspepsia, abnormal liver function test,alkaline, phosphatase increased, anorexia, flatulence, bilirubinemia
Hemic and lymphatic system:	eosinophilia, leukopenia
Metabolic and nutritional disorder:	creatinine increased, BUN (urea) increased
Musculo Skeletal system:	arthralgia (joint pain)
Nervous system:	Head ache, dizziness, insomnia, agitation, confusion
Skin and appendages:	pruritus, maculopapular rash, urticaria
Special senses:	taste perversion
Incidence of frequency 0.01%<0.1%	
Cardiovascular system:	tachycardia, migraine, syncope (fainting) vasodilatation (hot flushes)
Digestive System	moniliasis (oral), jaundice, Cholestatic jaundice, pseudomembranous colitis
Hemic and lymphatic system:	anaemia, leucopenia (granulocytopenia), leucocytosis, altered prothrombin values, Thrombocytopenia, thrombocytemia (thrombocytosis)
Hypersensitivity	allergic reaction, drug fever, anaphylactoid (anaphylactic) reaction
Metabolic disorders:	edema (peripheral, vascular, face), hyperglycaemia
Musculo Skeletal system:	myalgia (muscular pain), joint disorder (joint swelling)
Nervous system:	hallucination, sweating, paresthesia (peripheral paralgesia), anxiety, abnormal dreams (night mares), depression, tremor (trembling), convulsion
Respiratory system:	dyspnea, larynx edema
Skin and appendages:	photosensitivity reaction
Special senses:	tinnitus transitory deafness (especially at high frequencies), abnormal vision (visual disturbances), diplopia, chromatopsia, taste loss (impaired taste)
Urogenital system:	acute kidney failure, kidney function abnormal, vaginal moniliasis, hematuria, crystalluria, interstitial nephritis
Incidence of frequency <0.01%	
Cardiovascular system:	Vasculitis (petechiae, haemorrhagic bullae, papules, crust formation
Digestive System	moniliasis (gastrointestinal), hepatitis,
Hemic and lymphatic system:	hemolytic anaemia
Hypersensitivity:	Shock (anaphylactic, life threatening), pruritic rash
Nervous system:	grand mal convulsion, abnormal (unsteady) gat
Skin and appendages:	petechia, erythema multiforme (minor), erythema nodosum
The most common Adverse Reactions that has been reported based on Spontaneous reports sorted by body system and terms .	
Incidence of frequency <0.01%	
Digestive System:	liver necrosis (very rarely progressing to life threatening hepatic failure), Life threatening pseudomembranous colitis with possible fatal outcome
Hemic and lymphatic system:	petechia (punctuate skin hemorrhages), pancytopenia, agranulocytosis
Musculo-Skeletal system	tendinitis (predominantly achillo tendinitis); partial or complete tendon rupture (predominantly achilles tendon), exacerbation of symptoms of myasthenia gravis
Nervous system:	psychosis, intracranial hypertension
Skin and appendages:	Stevens-Johnson-Syndrome, epidermal neurolysis (Lyell-Syndrome)
Hypersensitivity:	serum sickness like reaction
Special senses:	Parosmia (impaired smell), Anosmia (usually reversible upon discontinuation)

DRUG INTERACTION:

The simultaneous administration of ciprofloxacin (oral) and iron, sucralfate or antacids and highly buffered drugs (e.g. antiretrovirals), containing magnesium, aluminium, or calcium reduces the absorption of ciprofloxacin. Consequently, ciprofloxacin should be administered either 1-2 hours before, or at least 4 hours after these preparations.

The concurrent administration of dairy products or fortified drinks alone (e.g. milk, yoghurt, calcium fortified orange juice) and ciprofloxacin should be avoided because absorption of ciprofloxacin may be reduced.

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

Absorption of the ciprofloxacin tablet was slightly diminished (20%) when given concomitantly with omeprazole.

Tizanidine:

Ciprofloxacin is an inhibitor of cytochrome P450 1A2 (CYP1A2)-mediated metabolism, coadministration with CYP1A2-metabolized tizanidine results in increased tizanidine plasma concentrations that could lead to clinically significant adverse events. In a pharmacokinetic study, systemic exposure of tizanidine (4 mg single dose) was significantly increased (Cmax 7-fold, AUC 10-fold) when the drug was given concomitantly with ciprofloxacin (500 mg bid for 3 days). The hypotensive and sedative effects of tizanidine were also potentiated.

Concomitant administration of tizanidine and ciprofloxacin is contraindicated.

Duloxetine:

ciprofloxacin is an inhibitor of cytochrome P450 1A2 (CYP1A2)-mediated metabolism, coadministration with CYP1A2-metabolized duloxetine results in increased plasma concentrations that could lead to clinically significant adverse events.

This restriction does not apply to antacids belonging to the class of H2 receptor blockers.

Concurrent administration of ciprofloxacin and theophylline can cause an undesirable increase in the serum theophylline concentration. This can lead to theophylline-induced side effects; in very rare cases these side effects can be life threatening or fatal. If concurrent use of the two products is unavoidable, the serum theophylline concentration should - therefore be checked and the theophylline dose appropriately reduced.

It has been reported that in animal the combination of very high doses of quinolones (gyrase inhibitors) and certain non-steroidal anti-inflammatory agents (but not acetylsalicylic acid) can provoke convulsions.

A transient rise in the concentration of serum creatinine was observed when ciprofloxacin and cyclosporin were administered simultaneously. Therefore, it is necessary to control the serum creatinine concentrations in these patients frequently (twice a week).

After simultaneous administration of ciprofloxacin and warfarin it has been reported that this may intensify the action of warfarin. In particular cases, concurrent administration of ciprofloxacin and glibenclamide can intensify the action of glibenclamide (hypoglycaemia).

It has been reported that probenecid interferes with renal secretion of ciprofloxacin. Co-administration of probenecid and ciprofloxacin increases the ciprofloxacin serum concentrations.

It has been reported that metoclopramide accelerates the absorption of ciprofloxacin (oral) resulting in a shorter time to reach maximum plasma concentrations. No effect on the bioavailability of ciprofloxacin has been reported.

DOSAGE AND ADMINISTRATION:

Unless otherwise prescribed, the following guideline doses are recommended:

Respiratory tract infection (according to severity and organism)	2 x 250-500 mg
Urinary tract Infections: - acute, uncomplicated - cystitis in women (before menopause) - complicated	 2x125 mg to 1-2 x 250 mg single dose 250 mg 2 x 250-500 mg
Gonorrhoea - extra genital - acute, uncomplicated	 2 x 125 mg single dose 500 mg
Diarrhoea	1-2 x 500 mg
Other infections (see Indications)	2 x 500 mg
Particularly severe, life threatening infections, i.e. -Streptococcal pneumonia -Recurrent Infectious in cystic fibrosis -Bone and joint infections -Septicaemia. -Peritonitis In particular when Pseudomonas, Staphylococcus or Streptococcus is present	 2 x 750 mg

Method of administration: -

The tablets are swallowed whole with a small amount of fluid.

They can be taken independent of mealtimes, (if the tablets are taken on an empty stomach, the active substance is absorbed more rapidly).

If the patient is unable to take tablets, because of the severity of the illness or for other reasons, it is recommended to commence the therapy with an intravenous form of ciprofloxacin. After intravenous administration the treatment can be continued orally.

Duration of treatment:

The duration of treatment depends on the severity of the illness and on the clinical and bacteriological course. It is essential to continue therapy for at least 3 days after disappearance of the fever or of the clinical symptoms. Mean duration of treatment:

- 1 day for acute uncomplicated gonorrhoea and cystitis,
- up to 7 days for infections of the kidneys, urinary tract, and abdominal cavity,
- Over the entire period of the neutropenic phase in patients with weakened body defenses,
- a maximum of 2 months in osteomyelitis. .
- and 7-14 days in all other Infections

In streptococcal infections the treatment must last at least 10 days because of the risk of late complications.

Infections caused by Chlamydia should also be treated for a minimum of 10 days.

Elderly

Elderly patients should receive a dose as low as possible depending on the severity of their illness and the creatinine clearance.

Children: contraindicated

Renal and hepatic Impairment

1. Impaired renal function
   - 1.1 Where creatinine clearance is between 31 and 60 ml/min/1.73m^2 or where the serum creatinine concentration is between 1.4 and 1.9 mg/10cml the maximum daily dose should be 1000 mg per day for oral administration.
   - 1.2 Where creatinine clearance is equal or is less than 30 ml/min/1.73m2 or where the serum creatinine concentration is equal or higher than 2.0 mg/100 ml the maximum daily dose should be 500 mg per day for oral administration.
2. Impaired renal function + haemodialysis
   Dose as in 1.2; on dialysis days after dialysis.
3. Impaired renal function +CAPD
   Administration of ciprofloxacin film coated tablets as 1 x 500 mg film coated tablet.
4. Impaired liver function
   No dose adjustment is required.
5. Impaired renal and liver -function
   Dose adjustment as in 1.1 and 1.2

OVERDOSAGE:

In the event of acute, excessive oral overdosage, reversible renal toxicity has been reported. Therefore, apart from routine emergency measures, it is recommended to monitor renal function and to administer Mg- or Ca-containing antacids which reduce the absorption of ciprofloxacin. Only a small amount of ciprofloxacin (<10%) is removed from the body after haemodialysis or peritoneal dialysis.

Treatment should be symptomatic and supportive.

PHARMACOLOGICAL CLASSIFICATION:

Antibacterial

STORAGE CONDITION:

Store below 30^{o}C, protected from light & moisture.

PRESENTATION:

QUINTOR 500 mg tablet is available as white coloured, capsule shaped, film-coated tablet with bisecting line on one side. QUINTOR 500 mg tablets are packed in Alu/PVC blister of 10 tablets. Such blisters containing 10 tablets are packed into a carton of 10's, 30's and 100's.

Not All presentations may be available locally.

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torrent PHARMA

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