CIPROX TABLET 250mg
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AVEX

Composition

Each tablet contains equivalent to Ciprofloxacin 250 mg

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Product Description

White oblong, 14.3 x 6.3 mm, film coated tablet, scored on both side

White oblong, 17.3 x 8.3 mm, film coated tablet, scored on both side

Pharmacodynamics

Ciprofloxacin is a synthetic 4-quinolone derivative, with bactericidal activity. It acts via inhibition of bacterial DNA gyrase, ultimately resulting in interference with DNA function. Ciprofloxacin is highly active against a wide range of Gram-positive and Gram-negative organisms and has shown activity against some anaerobes, Chlamydia spp. and Mycoplasma spp. Ciprofloxacin is also suitable for use in combination with penicillins, cephalosporins, aminoglycosides and tetracyclines where additive behaviour is usually observed.

Pharmacokinetics

Absorption of ciprofloxacin occurs rapidly, mainly from the small intestine (Abs. T1/2 = 2-15 min). Plasma levels are dose-related and peak 0.5-2.0 hrs after dosing. The AUC also increases dose proportionately after administration of both single and repeated oral doses. The oral bioavailability is approximately 70-80%. Distribution of ciprofloxacin within tissues is wide and the volume of distribution high, though slightly lower in the elderly.

Protein binding is low (between 19-40%). Elimination of ciprofloxacin and its metabolites occurs rapidly, primarily by the kidney. After single dose of ciprofloxacin, 55% are eliminated by the kidney and 39% in the faeces within 5 days. The elimination half-life of unchanged ciprofloxacin over a period of 24 - 48 hrs post dose is 3.1-5.1 hrs.

Even though, studies with severely renally impaired patients (creatinine clearance < 20ml/minute) do not give clear indications, it is recommended to reduce by half the total daily dose.

Results of studies in paediatric cystic fibrosis patients have shown dosages of 20 mg/kg orally twice daily is recommended to achieve plasma concentration/time profiles comparable to those achieved in the adult population at the currently recommended dosage regimen.

Indication

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

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 eyes.
- Infections of the kidneys and/or the efferent urinary tract.
- Infections of the genital organs, including gonorrhoea, prostatitis.
- Infections of the abdominal cavity (eg, biliary tract, peritonitis).
- Infections of the skin and soft tissue.
- Infections of the bones and joints.
- Infections or imminent risk of infection (prophylaxis) in patients whose immune system has been weakened (eg, patients on immunosuppressants or have neutropenia).
- Acute bacterial rhinosinusitis*
- Nosocomial pneumonia / Hospital-acquired pneumonia*
- Acute otitis media*
- Septicemia*
- Uncomplicated acute cystitis / Uncomplicated cystitis*

* Ciprox should be only used:

- When Pseudomonas is considered AND patient is allergic to antipseudomonal penicillins/cephalosporins;
- For resistant organisms with no other alternative antibiotics available.

Recommended Dose

The following guideline doses are recommended:

	Tablets
Respiratory tract infection (according to severity and organism)	2x250 - 500 mg
Urinary tract infections: - Acute, uncomplicated	2x125 mg to 1 - 2x250 mg
- Cystitis in women (before menopause)	single dose 250 mg
- Complicated	2x250 - 500 mg
Gonorrhea - Extragenital	2x125mg
- Acute, uncomplicated	single dose 250 mg
Diarrhea	1-2x500 mg
Other infections	2x500 mg
Particularly severe, life-threatening infections ie, - Streptococcal pneumonia - Recurrent infections in cystic fibrosis - Bone and joint infections - Septicemia - Peritonitis In particular when Pseudomonas, Staphylococcus or Streptococcus is present	2x750 mg

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.

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 gonorrhea 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 defences; a maximum of 2 months in osteomyelitis; 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.

Impaired Renal Function: Where creatinine clearance is between 31 and 60 mL/min/1.73 m^2 or where the serum creatinine concentration is between 1.4 and 1.9 mg/100 mL the maximum daily dose should be 1000 mg/day. Where creatinine clearance is $\leq$ 30 mL/min/1.73 m^2 or where the serum creatinine concentration is $\geq$ 2 mg/100 mL the maximum daily dose should be 500 mg/day.

Impaired Renal Function + Haemodialysis: Dose as Impaired Renal Function; on dialysis days after dialysis.

I*mpaired Renal Function + CAPD:* 500 mg

Impaired Liver Function: No dose adjustment is required.

Impaired Renal and Liver Function: Dose adjustment as in Impaired Renal Function.

Mode of Administration

Oral

Contraindication

- In patients who have shown hypersensitivity to ciprofloxacin or other quinolones
- In children/adolescents except in cases of cystic fibrosis associated (5-17 yrs)
- Pregnancy and lactation

Warnings and Precautions

The use of Ciprox should be avoided in patients who have experienced serious adverse reactions in the past when using fluoroquinolones containing products (see section Adverse Effects/Undesirable Effects). Treatment of these patients with Ciprox should only be initiated in the absence of alternative treatment options and after careful benefit/risk assessment.

Ciprox should be used with caution in patients suffering from epilepsy and CNS disorders. Crystalluria related to the use of ciprofloxacin has been reported.

Patients with a family history of or actual defects in glucose-6-phosphate dehydrogenase activity are prone to haemolytic reactions with quinolones.

Patients should avoid prolonged exposure to strong sunlight or UV radiation during treatment. Ciprox could result in impairment of the patient's ability to drive or operate machinery, particularly in conjunction with alcohol.

Particular caution is advised in patients who need to concurrently take: antacids, any other preparations containing aluminium, calcium, magnesium or iron, anticoagulants (such as warfarin), medicines used to relieve pain and inflammation except aspirin, glibenclamide, probenecid or metoclopramide, cyclosporin, phenytoin.

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.

Aortic aneurysm and dissection

Epidemiologic studies report an increased risk of aortic aneurysm and dissection after intake of fluoroquinolones, particularly in the older population. Therefore, fluoroquinolones should only be used after careful benefit-risk assessment and after consideration of other therapeutic options in patients with positive family history of aneurysm disease, or in patients diagnosed with pre-existing aortic aneurysm and/or aortic dissection, or in presence of other risk factors or conditions predisposing for aortic aneurysm and dissection (e.g. Marfan syndrome, vascular Ehlers-Danlos syndrome, Takayasu arteritis, giant cell arteritis, Behcet's disease, hypertension, known atherosclerosis).

In case of sudden abdominal, chest or back pain, patients should be advised to immediately consult a physician in an emergency department.

Prolonged, disabling and potentially irreversible serious adverse drug reactions

Very rare cases of prolonged (continuing months or years), disabling and potentially irreversible serious adverse drug reactions affecting different, sometimes multiple body systems (musculoskeletal, nervous, psychiatric and senses) have been reported in patients receiving fluoroquinolones irrespective of their age and pre-existing risk factors. Ciprox 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.

Tendinitis and tendon rupture

Tendinitis and tendon rupture (especially but not limited to Achilles tendon), sometimes bilateral, may occur as early as within 48 hours of starting treatment with 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 (above 60 years of age), with renal impairment, patients with solid organ transplants, and those treated concurrently with corticosteroids*. Therefore, concomitant use of corticosteroids should be avoided.

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

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 Ciprox should be advised to inform their doctor and pharmacist prior to continuing treatment if symptoms of neuropathy such as pain, burning, tingling, numbness, or weakness develop in order to prevent the development of potentially irreversible condition (see section Adverse Effects/Side Effects).

Psychiatric reactions

Psychiatric reactions may occur even after the first administration of fluoroquinolones, including Ciprox. In rare cases, depression or psychotic reactions can progress to suicidal ideations/thoughts and self-injurious behaviour, such as attempted or completed suicide (see section 'Undesirable effects'). In the event that the patient develops these reactions, Ciprox should be discontinued and appropriate measures instituted. Caution is recommended if Ciprox is to be used in psychotic patients or in patients with a history of psychiatric disease.

Interactions

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 2 products is unavoidable, the serum theophylline concentration should therefore be checked and the theophylline dose appropriately reduced. Animal studies have shown that the combination of very high doses of quinolones (gyrase inhibitors) and certain nonsteroidal 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).

The simultaneous administration of ciprofloxacin and warfarin may intensify the action of warfarin. In particular cases, concurrent administration of ciprofloxacin and glibenclamide can intensify the action of glibenclamide (hypoglycaemia). Probenecid interferes with renal secretion of ciprofloxacin. Co-administration of probenecid and ciprofloxacin increases the ciprofloxacin serum concentrations.

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. Therefore, patients under methotrexate therapy should be carefully monitored when concomitant ciprofloxacin therapy is indicated.

The simultaneous administration of ciprofloxacin and iron, sucralfate or antacids and highly buffered drugs (eg, didanosine tablets), containing magnesium, aluminium, or calcium reduce the absorption of ciprofloxacin. Consequently, ciprofloxacin should be administered either 1-2 hrs before, or at least 4 hrs after these preparations. This restriction does not apply to antacids belonging to the class of H_2-receptor blockers.

Metoclopramide accelerates the absorption of ciprofloxacin resulting in a shorter time to reach maximum plasma concentrations. No effect was seen on the bioavailability of ciprofloxacin.

Pregnancy and Lactation

Ciprox during pregnancy is not recommended. Studies have indicated that ciprofloxacin is secreted in breast milk. Administration to nursing mothers is thus not recommended.

Adverse Reactions / Side Effects

Usual side effects are diarrhoea, nausea and skin rashes.

Rare side effects reported include: Allergic reactions (e.g. angioedema), hyperglycaemia, gastrointestinal reactions (e.g. vomit, indigestion, anorexia, pseudomembranous colitis), skin sensitivity to the sun, haematological disturbances (e.g. anaemia, eosinophilia), hepatitis, yellow jaundice, crystalluria, or visual disturbances, nervous system disorders* (e.g. headache, dizziness, tremor, depression), psychiatric disorders*, eye disorders*, ear and labyrinth disorders*, general disorders and administrative site conditions*, musculoskeletal & connective tissue disorders* (e.g. arthralgia, myalgia).

Psychiatric disorders

Rare: Depression (potentially culminating in suicidal ideations/ thoughts or suicide attempts and completed suicide)

Very Rare: Psychotic reactions (potentially culminating in suicidal ideations/ thoughts or suicide attempts and completed suicide)

* 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 tendinitis, tendon rupture, arthralgia, pain in extremities, gait disturbance, neuropathies associated with paraesthesia, depression, fatigue, memory impairment, sleep disorders, and impairment of hearing, vision, taste and smell) have been reported in association with the use of fluoroquinolones in some cases irrespective of pre-existing risk factors (see section Warnings and Precautions).

Post Marketing Experience

Exacerbation of myasthenia gravis.

Overdose

Routine emergency measures and to monitor renal function, including urinary pH and acidify, if required, to prevent crystalluria. Patients must be kept well hydrated and, in the case of renal damage resulting in prolonged oliguria, dialysis should be initiated. Calcium or magnesium antacids may be administered as soon as possible after ingestion of Ciprofloxacin tablets in order to reduce the absorption of ciprofloxacin. Serum levels of ciprofloxacin are reduced by dialysis.

Storage Condition

Store below 30˚C in a dry place protected from light.

Pack Size

Blisters of Aluminum/PVC pack 10X10 tablets

Manufacturer

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