For the use of a Registered Medical Practitioner or a Hospital or a Laboratory.

C-FLOX 250 & 500

(Ciprofloxacin tablets 250 mg & 500 mg)

C-flox (Ciprofloxacin) is a broad spectrum and potent synthetic fluoroquinolone antibacterial agent. It is indicated in various respiratory, urinary and other infections caused by susceptible microorganisms.

Description: C-flox 250: White to off white coloured, round, biconvex, film coated tablet plain on one side and bisecting line on other side of the tablet.

C-flox 500: White to off white coloured, capsule shaped, biconvex, film coated tablet with break line on one side of the tablet.

Clinical Pharmacology: Ciprofloxacin exhibits potent bactericidal action by Interfering with enzyme DNA gyrase -which is needed for the synthesis of bacterial DNA. The in vitro antimicrobial spectrum of Ciprofloxacin includes wide range of microorganisms including Gram-negative bacteria like campylobacter jejuni, E.coli, Citrobacters, H.influenzae, H.parainffuenzae, Shigella, Salmonella typhi, Vibrio cholerae, Neisseria-gonorrhoea, N.meningitidis, Branhaemella catanrhalis, Kleb.pneumoniae, Brucella melitensis, H.ducrayi, Proteus mirabilis, P.vulgaris, Pseudomonas aeruginosa, Providancia rettgeri, P. startii, Serratia marcescens, Enterobacter cloacae, and Gram-positive bacteria like Staphylococcus aureus, Staph. epidermidis, Staph.haemolyticus, Streptococcus pneumoniae, Streptococcus pyogens. ..; Most strains of Ps. cepacia, Ps.multophilia and most anaerobic bacteria are resistant to Ciprofloxacin.Ciprofloxacin is slightly less active at acidic pH. Ciprofloxacin does not cross- react with other antimicrobial agents. Synergism is reported with aminoglycosides, clindamycin, metronidazole and particularly beta-lactams. Ciprofloxacin is also shown to have post antibiotic effect (PAE) i.e. continued antibacterial effect after cessation of drug administration. Ciprofloxacin is rapidly and well absorbed from the gastrointestinal tract. Oral bioavailability is about 70% and a peak plasma concentration of about 2.5 mcg per ml is achieved 1 to 2 hours after a dose of 500 mg by mouth. Absorption is delayed in presence of food. Plasma protein binding ranges from 20 to 40%. Ciprofloxacin is widely distributed in the body and tissue penetration is generally good. High concentrations are achieved in bile. The plasma half-life is about 3.5 to 4.5 hours, and there is modest accumulation. Half life may be prolonged in severe renal failure. Ciprofloxacin is eliminated principally by urinary excretion and non-renal clearance accounts for one third of its elimination. Urinary excretion is by active tubular secretion and by glomerular filtration. Urinary excretion is reduced by Probenecid. Atleast 4 active metabolites are identified. Among which oxociprofloxacin is major urinary metabolite and sulphociprofloxacin the primary fecal metabolite. About 40 to 50% of an oral dose is excreted unchanged in the urine and about 15% as metabolites.

Indications: C-flox is indicated for the treatment of uncomplicated and complicated infections caused by pathogens sensitive to Ciprofloxacin: 1. 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. 2. Infections of the middle ear (otitis media), of the pranasal sinuses (sinusitis), especially if these are caused by gram-negative organisms including Pseudomonas or by Staphylococcus. 3. Infections of the eyes 4. Infections of the kidney and for the efferent urinary tract 5. Infections of the genital organs, including adnexitis, gonorrhea, prostatitis 6. Infections of the abdominal cavity (eg: infections of the gastrointestinal tract or of the biliary tract, peritonitis) 7. Infections of the skin and soft tissue 8. Infections of the bones and joints 9. Sepsis 10. Infections or imminent risk of infections (prophylaxis in patients whose immune system has been weakened (e.g patients on immunosuppressants or have neutropenia) 11. 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, Edwardseilla, Proteus (indole-positive and indole-negative), Providencia, Morganella, Yersinia; Vibrio, Aeromonas, Plesiomonas, pasteurella, haemophilus, campylobacter, Pseudomonas, legionelia, Nesseria, Moraxella, Acinetobacter, Brucella; Staphylococcus, Listeria, Corynebacterium, Chlamydia.

The following show varying degrees of sensitivity: Gardnereila, Flavobacterium, Alcaligenes, Streptococcus agalactiae, Enterococcus faecalis, Streptococcus pneumonia, 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.

Dosage and Administration: Adults: Unless otherwise prescribed, the following guideline doses are recommended: Respiratory tract infection (according to severity and organism): 2 X 250 - 500 mg Acute, uncomplicated Urinary tract infections:: 2 X 125 to 1-2 X 250 mg Cystitis In women (before menopause): single dose 250 mg Complicated Urinary tract infections: 2 X 250-500 mg Extragenital Gonorrhea: 2 X 125 Acute, uncomplicated Gonorrhea: single dose 250 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 infections in cystic fibrosis, bone and joint infections, septicemia, peritonitis. In particular when Pseudomonas Staphylococcus or Streptococcus is present: 2 X 750 mg

Route and Method of Administration: Oral. 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 the clinical symptoms. Mean duration of treatment: -1 day for acute uncomplicated gonorrhea and cystitis. - up to 7 days for infections of the kidney, urinary tract and abdominal cavity. - over the entire period of the neutropenic phase with weakened body defenses. - 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. 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/100 ml , the maximum daily dose should be 1000 mg per day for oral administration

1.2 Where creatinine clearance is equal or less than 30 ml/min/1.73m^2 or where the serum creatinine concentration is equal or higher than 2.0mg/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 or 2 X 250 mg film coated tablets. 4. Impaired liver function: No dose adjustment is required 5. Impaired renal and liver function: Dose adjustment as in 1.1 and 1.2

Contraindications: Ciprofloxacin is contraindicated in cases of hypersensitivity to Ciprofloxacin or other quinolone chemotherapeutics. Ciprofloxacin must not be prescribed for children, adolescents, since there is no experience on the drug's safety in these patients groups and since, on the basis of animal studies, it is not entirely improbable that the drug could cause damage to articular cartilage in the immature organism.

Precautions & Warnings: Gastro intestinal 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 (eg: vancomycin, orally, 4 X 250mg/day). Drugs that inhibit peristalsis are contraindicated. There can are be temporary increase in transaminase, alkaline phosphatase or cholestatic jaundice, especially in patients with previous liver damage.

Nervous System: In patients of epilepsy and those having history of CNS-disorders (eg: 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. In rare cases depression or psychosis can progress to sell endangering behaviour. In these cases ciprofloxacin should be discontinued and the doctor should be informed immediately.

Hypersensitivity: There have been instances where the hypersensitivity and allergic reactions occurred after the first administration of ciprofloxacin. In such cases the doctor should be informed immediately. Anaphylactic /anaphytactoid reactions in very rare instances can progress to a life threatening shock, after the first administration. In these cases ciprofloxacin has to be discontinued, medical treatment (eg: treatment for shock) is required.

Musculo-skeletal System: At any sign of tendinitis (eg: painful swelling) the administration of ciprofloxacin should be discontinued, physical exercise should be avoided, and a physician should be consulted. Tendon rupture (predominantly achilles tendon) has been reported predominantly in elderly on prior treatment with glucocorticoids.

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 (ie: sun-burn like skin reactions) occurs.

Ability to drive and use machines: Even when 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.

Use in Pregnancy, Lactation & Children: It is not used in pregnancy. It is excreted into breast milk. Safety and effectiveness of C-flox has not been established in children.

Interactions with other drugs: The simultaneous administration of ciprofloxacin (oral) and iron, sucralfate or antacids and highly buffered drugs (eg: antiretrovirals), containing magnesium, aluminium or calcium reduce the absorption of ciprofloxacin. Consequently ciprofloxacin should be administered either 1-2 hours before, or at least 4 hours after these preparations. This restriction does not apply to antacids belonging to the class of H2 receptor blockers. Concurrent administration of ciprofloxacin and theophylline can cause 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 used of the two 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 non-steroidal anti-inflammatory agents (but not acetylsalicyclic 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.

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

Side Effects

The following side effects have been observed:

Effects on the gastrointestinal tract

Nausea, diarrhoea, vomiting, digestive disturbances, abdominal pain, flatulence, loss of appetite. If severe and persistent diarrhoea occurs during or after treatment, the doctor must be consulted since this symptom can hide a serious underlying intestinal disorder (pseudomembranous colitis) which requires immediate treatment. In such cases C-Flox must be discontinued and suitable therapy initiated (e.g 4 x 250 mg Vancomycin/day p.o). Antiperistaltics are contraindicated.

Effects on the nervous system

Dizziness, headache, tiredness, sleeplessness, agitation, tremor; very rarely: peripheral paralgia, sweating, unsteady gait, convulsions, anxiety states, nightmares, confusion, depression, hallucinations, taste and smell impairment, visual disturbances (e.g double vision, seeing colours). These reactions sometimes occurred after only one dose. In such cases C-Flox must be discontinued immediately and the physician must be informed.

Hypersensitivity reactions

Skin reactions such as rashes. Very rarely: • Pruritis, drug fever - Anaphylactic/anaphylactoid reactions (eg: facial, vascular and laryngeal oedema; dyspnoea right through to life threatening shock), sometimes after only one dose. In such cases, C-Flox must be discontinued immediately; medical treatment (eg: shock therapy) is necessary. • Pinpoint haemorrhages (petechlae), haeinorrhagic vesicles (haemorrhagic bullae), and small nodules (papules) with incrustation indicative of vascular involvement (vasculitis), Stevens-Johnson syndrome, interstitial nephritis, hepatitis, liver cell necrosis right through to life threatening liver failure.

Effects on the cardiovascular system Very rarely: tachycardia, hot flushes, migraine. syncope.

Others

Very rarely: articular complaints, general feeling of weakness, muscular pains, tendovaginitis, slight photosensitivity, transient impairment of kidney function right through to temporary kidney failure, tinnitus, temporary loss of hearing, particularly at high frequencies.

Effects on the blood and blood constituents

Eosinophilia, leucocytopenia,. leucocytosis, anaemia; very rarely: thrombocytopenia, thrombocytosis, altered prothrombin values

Influence on laboratory parameters urinary sediment

Transient increases in transaminases and alkaline phosphatase can occur, as well as cholestatic jaundice, especially in patients with existing liver damage; transient increases in serum urea, creatinine and bilirubin, hyperglycaemia; in isolated cases crystaluria and haematuria. Even when used in accordance with the instruction this product can affect the speed of reaction to such a degree that the ability to drive or to operate machinery is impaired. The effect is intensified by combination with alcohol.

Overdosage: Information on overdosage with C-flox is not available. In the event of acute overdosage, stomach should be emptied by inducing vomiting or by gastric lavage. The patient should be carefully observed and given supportive treatment in the form of adequate hydration. Only a small amount (<10%) is removed from the body after haemodialysis or peritoneal dialysis.

Presentation: C-flox 250 & C-flox 500 tablets are available In strip of 10 tablets and 10 such strips packed in a printed box.

Storage condition: Store below 30°C in a dry place.

Shelf life: Four years from the date of manufacturing.

Date of information: Feb 2019

Registration Holder: JETPHARMA SDN BHD

Manufactured by:
INTAS
INTAS PHARMCEUTICALS LTD.
Matoda-382 210, Dist.: Ahmedabad. INDIA

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Front Side

Back Side

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